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SWEAT GLAND CANCER OF THE BREAST

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SWEAT gland cancer of the breast has been considered a clinico-pathological entity for many years at the Memorial Hospital. We have correlated this microscopical diagnosis with clinical findings so that it is now possible, in a considerable percentage of cases, to make a correct clinical diagnosis of sweat gland carcinoma of the breast prior to operation. The peculiar histological features of these carcinomata and their relationship to certain mammary cysts and even analogous normal structures found in almost every breast, are significant from the standpoint of histogenesis.

It is generally conceded that the breast is of sweat gland origin. It is not unusual to observe the reproduction of primitive structures by malignant neoplasms in any organ. Some mammary cancers show this morphological resemblance to sweat glands in such a degree, that we feel justified in terming them sweat gland carcinomata.

The evidence leading to this conclusion can best be introduced by reviewing the development of the breast as a modified sweat gland, the anatomical and physiological analogies of the adult breast to sweat glands, and the phylogenetic relation of the breast to sweat glands as shown in comparative anatomical studies. Following this indirect argument, we shall present more direct proof of this origin by data accumulated from histological studies or normal, cystic, and cancerous breasts.

THE DEVELOPMENT OF THE BREAST AS A MODIFIED SWEAT GLAND

It is our contention that the mammary glands and sweat glands are homologous structures, which develop from a common primitive tubular type of epidermal gland. The breast is without doubt a cutaneous gland and has been structurally and functionally considered as such by anatomists and physiologists. Vertebrates possess two types of

Fig. 4. Serial sections through an anastomosis of a sweat gland duct (apocrine type) with a lacteal duct of the breast. Note the characteristic differences in epithelium; the lacteal duct is lined by orderly, flat, cuboidal cells with lilac-colored neutrophilic cytoplasm; the apocrine sweat gland duct is lined by irregular, club-shaped, high columnar cells with markedly eosinophilic cytoplasm. The intraductal papillary tufts and the dichotomous branching of the lumen to form a racemose type of gland is also seen in the apocrine sweat glands of axilla and groin but are not in the more generally distributed and simple tubular glands of the exocrine type. Practically all of the sweat gland structure in the breast can be found to empty into lacteal ducts, if careful serial sections are made. If such a sweat gland system is not aberrant and congenital (as we suspect it to be) but a metaplasia, there are phylogenetic reasons for assuming this change to be an atavistic throw-back to the sweat gland origin of the breast. It is significant that this transition is sharp and clearly shown at the site of anastomosis and that the characteristic morphological features are retained in every part of this sweat gland duct and its branches.

Fig. 8. Diffuse adenomatosis of breast, classified as precancerous. Here and in the normal and mastitic breast are islands and even complete lobules of sweat gland tubules. The sweat gland adenomatosis in the center of a lobule of lacteal gland adenomatosis may indicate that this change is metaplastic.

skin glands which are classified morphologically as acinous and tubular glands. Functionally they are divided into sebaceous and sweat glands. The breast is a modified sweat gland.

In an early stage of the embryo the ventrolateral surfaces of the body show a broad linear band of high epithelium generally known as "Schwalbe's milk streak." The first anlage of the breast in humans appears in the last half of the second month of fetal life. Numerous puctuate epithelial thickenings are visible along the milk streak. They are known as milk points or mammary fields and consist of circumscribed epidermic proliferations in the shape of a tiny mound. These milk points are quite prominent in human embryos ranging from 28 to 60 millimeters in size. In so much as only one pair of breasts are ordinarily present in newborn and adult humans, the other anlagen are presumably those of supernumerary breasts, because they are of similar histological make-up and correspond to the natural locations of aberrant breast tissue when it does occur. In the early stages of development, the mammary gland corresponds very closely to the origin and differentiation of sudoriparous glands. The sweat glands adjacent to the breast appear much later in the embryo, but in significantly close relationship. The primitive breast differs from the early sweat glands only in the exceptional size of its tubules.

In the fifth month of fetal life, the lentil shaped plaques in the malpighian layer of the epidermis, which we have referred to as milk points, begin to invaginate and dip down into the underlying connective tissue as solid cords which later acquire lumens. The milk point contains a basal layer of cylindrical cells with oval nuclei, the longitudinal axes of which are in a vertical plane. External to these cells are several rows of small polygonal cells with round nuclei. These solid cellular cord-like proliferations originate from the cylindrical cells in the superficial epidermic plaques. These proliferations become club shaped and extend farther downward into the connective tissue where they branch off into similar solid secondary buds. In the meantime, the connective tissue surrounding these cords thickens and forms areolar tissue. At this stage in the development of the breast, the tubules do not differ from the ducts of the meibomian glands, the early hair follicles, or the sweat glands. The primary cords or tubules later develop hair follicles with corresponding sebaceous glands, and the secondary buds divide into the ducts of the breast proper. These ducts extend deeply into fatty tissue which is arranged in embryonic fat islands. Toward the end of fetal life there is formed in many places, especially in the middle part of the tubule, a differentiation of the layers corresponding to those of the large sweat glands so that eventually the ducts contain two layers of cells, an inner secretory layer and a basal layer such as in the adult gland. The blind tubules in the resting stage do not show the typical acinous structure until later life, when they become functional.

Kolliker and Benda are both agreed that the breast is of sweat gland origin. The abundant histological evidence in the breast justifies this belief. Rudimentary sweat gland structures can be found in almost every breast, if diligent search be made. Some of the tubules of sweat gland origin developing beneath the areola of the breast empty into the mammary ducts, rather than on the surface of the skin, in a manner similar to the primitive hair follicles. The hair on the glandular field usually disappears in the progress of development together with the accompanying sebaceous glands. The sweat glands may or may not remain; if they do, they retain their ordinary relation to the lacteal ducts. This anatomical arrangement, as will be shown later, accounts for the occasional occurrence of sweat gland adenomata and carcinomata immediately beneath the nipple.

There are at least five different interpretations of the significance and histogenesis of the so called sweat gland anomalies in the breast, either normal sweat glands, sweat gland cysts, or sweat gland tumors.

a. Extramammary sweat glands of the skin are said to be included accidentally in the tissues of the mammary gland as aberrant cell rests (Creighton).

b. The sweat gland structures represent an arrest in the development of the breast in

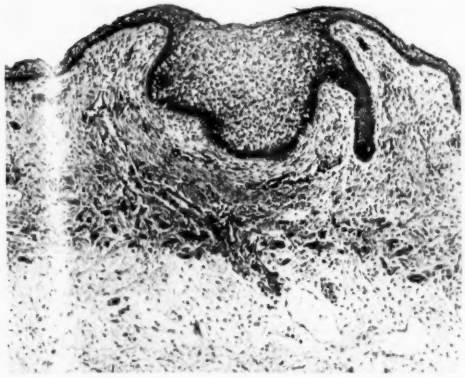

Fig. 1. Development of breast. Human embryo 14 centimeters in length. The milk point or anlage of the breast, showing it to be a cutaneous merocrine gland. Note the basal columnar cells and superjacent polygonal cells with round nuclei in the rudimentary nipple. The early lacteal bud is morphologically indistinguishable from a primitive sweat gland tubule.

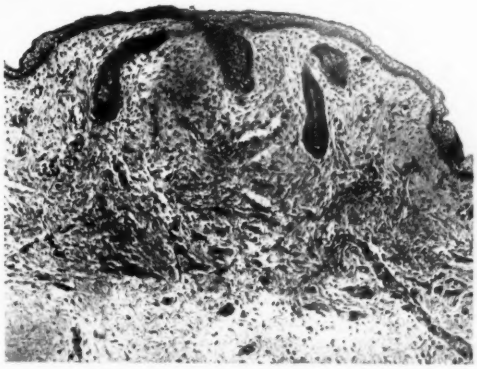

Fig. 2. Development of breast. Human embryo 14 centimeters in length. Another milk point, showing several lacteal ducts which have acquired lumens. At this stage, the resemblance to sweat gland tubules is obvious and significant.

these locations at a phylogenetically early stage, which we may call the sweat gland phase, i.e., incomplete mammary differentiation. Von Saar was first to correlate these structures with sweat glands; he believed that they indicate "a phylogenetic level at which the breast tissue had differentiated itself from sweat glands."

c. The sweat gland tubules, cysts, and tumors in the breast are atavistic phenomena due to metaplastic changes in the lacteal ducts, which become dedifferentiated into an embryologically earlier cell type (Prym, Dreyfuss).

d. True sweat glands are normally present in every breast, where they anastomose with and empty their secretions into the interlobular lacteal ducts (Ewing).

e. The pale epithelial cells comprising these structures are said to be entirely unrelated to sweat glands. The morphological changes and peculiar staining affinities are attributed to degeneration of these cells, in which they simulate but do not constitute sweat gland epithelium (Dawson).

It seems fundamentally unimportant to us to determine whether these peculiar mammary structures are anomalous, embryonal, normal, or degenerative. The major premise has been that the breast is a modified sweat gland; the appearance of apparent sweat gland tubules and cysts in the breast is a logical occurrence, even though the mode of origin remains in dispute. It is significant to us that the anatomical and staining characteristics of these cells remain through all the transitional phases of normal sweat gland tubules, cysts, intracystic papillomata, adenomata, and car-

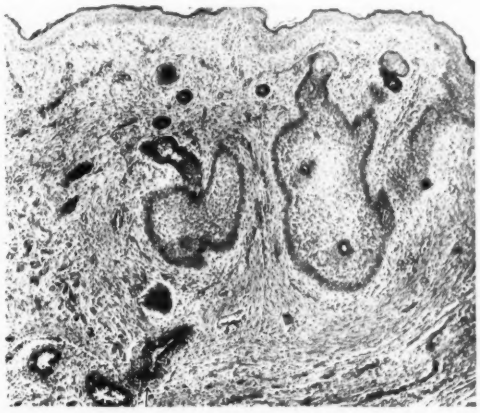

Fig. 3. Development of breast. Human embryo 33 centimeters in length. Intermediate differentiation of the breast. Serial section to show the early anastomosis of sebaceous glands with lacteal buds. These sebaceous glands and the numerous hair follicles seen at this stage are transitory and are not found in this close relationship in the fetus at term. At the base (arrow) a lacteal duct with two cells layers can be seen; it is of typical sweat gland structure.

Fig. 5. Cystic sweat gland tubules in a normal breast. The adjacent lacteal lobules stand out in marked contrast to the sweat gland tubules, because of the difference in size, structure, and staining qualities of the cells.

cinomata. This maintenance of cell type in the evolution of sweat gland tumors is a strong argument against the degenerative theory. Careful microscopical scrutiny of serial sections of these breasts frequently reveals the site of anastomosis of lacteal and sweat gland ducts. The abrupt transition in the character of epithelium lining these ducts is noteworthy; if the process were degenerative it would probably not be confined so exactly to this duct system. Our studies have confirmed the theories of Ewing in regard to the histogenesis of these structures.

One is impressed, in studying the structure of the developing mammary gland in the fetus, by the large size and abundance of sweat glands in the skin surrounding the breast. We believe it to be significant that the sweat glands of the newborn, as compared with the adult, are relatively enormously hypertrophied.

The development of the sweat glands in the skin corresponds in miniature to the development of the breast proper. The majority of sudoriparous glands originate on the finger tips, palms, and soles in the fourth month of fetal life. Their anlagen resemble closely those of the breast. They project downward as solid bulbous papillæ the terminations of which become tortuous in the sixth lunar month. Intercellular clefts appear in the seventh month to form a continuous lumen in the tubule. At this time the distal end of the tubule becomes convoluted as in the adult sweat gland. In the axillary and inguinal sweat glands the tubules branch and form secondary buds as they do in the breast. The epithelium of the sweat gland duct acquires two distinct layers, an inner large celled secretory layer and an outer flattened myo-epithelial layer. The number of sweat glands in the skin are definitely determined at birth as are the number of hairs.

ANATOMY AND PHYSIOLOGY OF THE ADULT BREAST AND ITS RELATION TO SWEAT GLANDS

We have previously stated that sweat gland tubules are found in almost every breast. They seem to be more common in subjects with oily skin and considerable body hair, and who are predisposed to acne and sebaceous cysts. The number of these sweat gland tubules in the breast is extremely variable. In some patients there are many and in others there are relatively few. Their locations in the breast correspond with the regional distribution of sweat gland cysts and sweat gland cancers in this organ, namely, in the axillary segment, submammary fold, and margins of the breast as well as immediately beneath the skin of the areola.

It appears evident that there are two types of ducts within the breast; the lacteal ducts which form the bulk of the functioning glandular tissue and the occasional irregularly distributed sweat gland ducts. Hereafter, in our discussion we shall employ the terms lacteal ducts and sweat gland ducts to distinguish these two structures. The investigator will find in serial sections of the breast that sweat gland ducts anastomose, in the majority of cases, with the normal lacteal ducts. The mammary gland never presents typical, entirely normal coiled sweat glands in its deeper structure. These sweat gland ducts represent various transitional stages from primitive sweat gland epithelium to normal lacteal epithelium. Such transitions may be observed in the ducts of the same breast.

Fig. 6. Two tiny cysts in a breast which is the seat of chronic cystic mastitis, or Reclus' disease. The cyst of the lacteal duct is lined by epithelial cells in two orderly layers, a basal germinating layer and an inner secretory layer. The cytoplasm of these cells is lilac colored and neutrophilic. The cyst in the adjacent sweat gland system in the breast illustrates the peculiar histologic features of hidradenoid cysts. The eosinophilia, the intracystic papillary tufts, the plication or infolding of the epithelial lining, and the disposition of the club-shaped columnar cells are practically never found in cysts of lacteal ducts, but are commonly observed in apocrine sweat gland cysts of the axilla, groin, and scrotum.

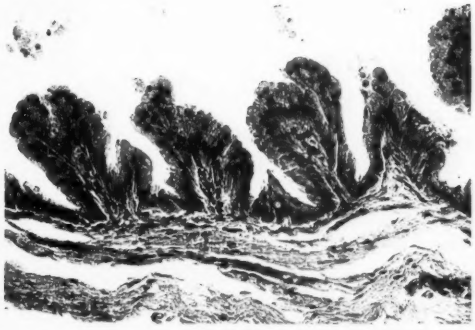

Fig. 7. High power magnification of wall of sweat gland cyst in Figure 6. The cytoplasm of the club-like columnar cells is granular and eosinophilic. The papillæ vary in size and structure, they commonly have sparse stroma, and occasionally they exhibit an arcade towering or stratification of epithelium. The so called myo-epithelial cells are not well shown in this section, but in the deeper tissue there can be seen a thin encircling band of smooth muscle fibers. Muscle tissue is not found in connection with lacteal cysts or ducts except in the region of the ductal ampullæ.

The lacteal ducts of the mammary gland are lined either by a single, or more frequently, a double row of columnar cells. They possess a relatively broad lumen. The membrana propria is supported by a connective tissue wall containing both longitudinal and circular elastic fibers, but no muscle. The outer row is lower than the inner one. On the contrary, there is only one epithelial cell layer in the alveoli, the structure of which differs during various functional states. Around the alveoli there may be found a small number of elongated stellate cells sending out long fine processes, the so called basket cells, the nature of which is in dispute.

The sweat gland ducts in the breast can easily be differentiated from the lacteal ducts by ordinary tissue staining. The inner secretory cell layer is not cuboidal or flat, but is composed of high columnar, stratified epithelium with a tendency to papillary formation which is never seen in normal lacteal ducts. These cells may be piled up on each other in the form of terraces. The staining peculiarities are quite striking. The cytoplasm contains fine granules which with eosin stain pink or even light red. This eosinophilia can best be appreciated in comparing sweat gland ducts and lacteal ducts in the same microscopical field. We are presenting a colored illustration showing this difference in the staining affinities of sweat gland epithelium and lacteal epithelium; in this picture, the sweat gland duct is seen emptying into a lacteal duct (Fig. 4, frontispiece). At the site of anastomosis the transition between eosinophilic cells and neutrophilic cells is abrupt. Sweat glands in the normal skin have eosinophilic cytoplasm, which characteristic of the sweat gland ducts in the breast substantiates to some extent the homologous origin of these structures. Goldzieher and Kaldor, on the other hand, interpret this eosinophilia as a metabolic change in the lacteal cell which causes it to simulate sweat gland epithelium; they offer no evidence, however, to substantiate their opinion.

Another anatomical analogy which exists between the sweat glands of the skin and the sweat gland structures within the mammary gland is the frequent association of smooth muscle cells with the membrana propria of sweat glands of the skin and sweat gland structures in the breast. There are no muscle cells visible in the lacteal ducts but surround-

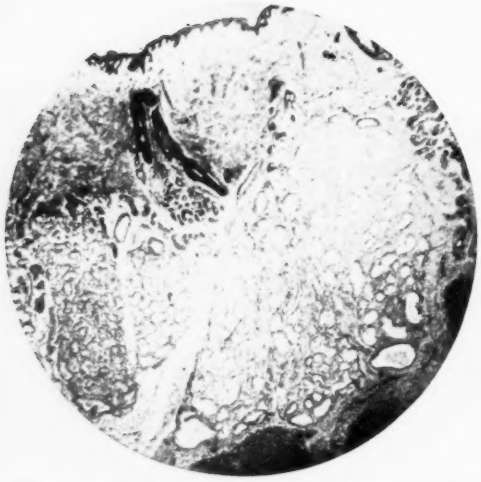

Fig. 9. Sweat gland adenoma in the skin overlying a carcinoma of the breast. The two tumors are adjacent but separate. The sweat gland tubules are enormously multiplied and cystic. This finding illustrates the consistent adherence to histogenic type in the benign and malignant sweat gland tumors of the breast (from Krompecher).

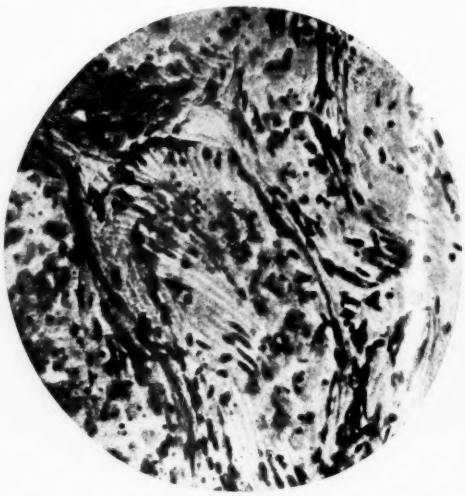

Fig. 10. Sweat gland adenoma in the skin overlying a carcinoma of the breast. The muscle fibers characteristic of sweat glands and their neoplasms are plainly visible. (From Krompecher.)

ing the acini of these ducts are the so called basket cells, first described by Langhans in 1873. These spindle or stellate cells are found side by side in parallel arrangement and are bounded on the outside by the structureless stratum of the membrana propria and on the inner side by the epithelial layer. Their occurrence in the terminal vesicles is denied by Creighton and Benda and asserted by Nagel and Kuru. They are interpreted as smooth muscle cells by Kuru, Heidenhain and Benda. A definite fibrillation can be made out in these cells similar to that seen in other muscle cells; their staining reaction is also considered characteristic of the latter. As to their function, it is believed to be that of contracting to express secretion from the ducts. In accordance with this view of their origin and character, they have been designated as myoepithelial cells. No cells of this character are visible surrounding the lacteal ducts proper, but they are so frequently found surrounding the sweat gland ducts in the breast and are such an integral part of the sweat glands of the skin, as to be considered characteristic of these structures. Kolliker in 1849 first demonstrated the presence of smooth muscle cells arising from the outer epithelium of the sweat gland ducts in the skin. Kolossow in 1896 found persistent structures corresponding to these muscle cells in the breast proper. This muscle network is best shown in the sweat glands of the snouts in many animals.

There has been considerable argument as to whether or not these cells are actually smooth muscle cells. Some histologists have doubted this theory of their nature and have assumed that they are cells corresponding to ordinary mesenchyme, which somehow have become closely approximated to the ducts and alveoli. Such a conception has been expressed more recently by Diechmann (1925). Others believe that these cells line capillary spaces running parallel to the wall of the ducts or cysts. Whatever their true character may be it seems significant that they are found fairly constantly in the sweat glands of the skin and are frequent in the sweat gland ducts of the breast. It was this analogy which prompted Benda to be the first to postulate the theory that the breast is a modified sweat gland. He found that the large sweat glands of the axilla and certain ducts in the mammary gland have in common an inner layer

Fig. 11. Wall of a sweat gland cyst in the breast. Immediately beneath the stratified epithelial cells are numerous fine muscle fibers, presumably of the myo-epithelial type. (From Krompecher.)

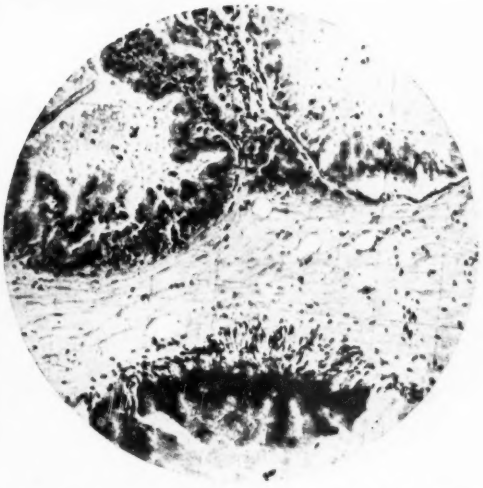

Fig. 12. Part of three sweat gland cysts of the breast. The "pale" columnar epithelial cells are shown in papillary and arcade formation. Radiating from the membrana propria of one of these cysts are many fine muscle fibers. (From Krompecher.)

of secreting epithelial cells and this outer layer of supposedly contractile muscle or myo-epithelial cells. The reason for the persistence of these peculiar cells in the sweat gland ducts of the breast and their absence in the lacteal ducts is that they represent a vestigial relic or survival of the earlier necessity for the contraction of ducts and expression of secretion which is not necessary in the human breast. Smooth muscle fibers are found within the nipple and within the adjacent portions of the areola of the normal breast. These are arranged in circular bundles at the base of the nipple, the longitudinal fibers within its substance diverging into radiating bundles within the subcutaneous tissues of the areolar zone. Contraction of these fibers elevates and hardens the nipple, thus simulating the action of erectile tissues. In some way, this phenomenon is related to the action of the muscle fibers surrounding the sweat glands of the skin and aiding the excretion of sweat.

The sweat glands of the areola lie deeper than the sebaceous and Montgomery glands. They are found in the loose connective tissue between the base of the nipple and the glandular portion of the breast proper. This tissue is traversed by the true lacteal ducts, 12 to 20 in number, and it is around these vertical ducts that the small sweat glands are distributed. As we have previously stated, they may at times empty into these lacteal ducts rather than on the surface of the nipple. Creighton found them uniformly in six breasts which he examined. Krompecher and later Colin found sweat gland adenomata arising in this location, and we have observed sweat gland carcinomata apparently arising from these structures.

In discussing the theory of sweat gland cancers of the breast and their relation to sweat glands of the breast, we have been questioned about the distribution of sweat glands in the mammary skin. They are most abundant in the submammary fold and in the axillary segment and their function of secreting sweat is related somewhat to the menstrual cycle of the patient. In many women the breasts become moist when the rest of the skin is dry; this is particularly true at the onset of the menstrual period, when the breasts enlarge, and the nipples readily become erect. In other words, the secretion of sweat on the breast and lactation by the breast are stimulated similarly by ovarian secretion. The activity of the sweat glands in the mammary skin was well

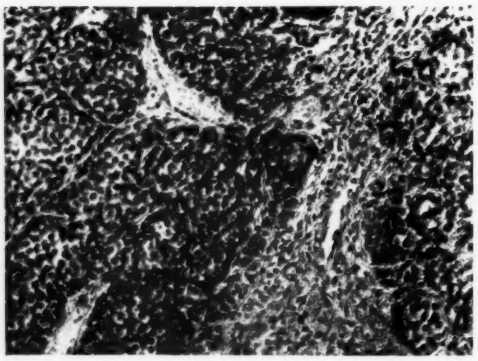

Fig. 13. Sweat gland carcinoma of skin of shoulder. Note the close histological resemblance to certain cellular or medullary varieties of mammary cancer.

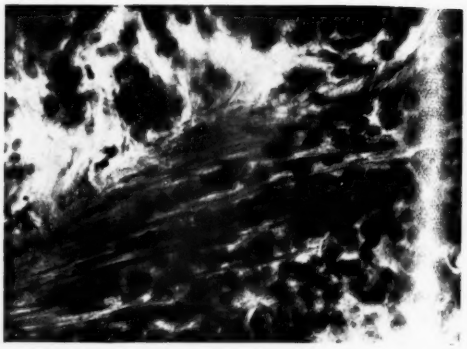

Fig. 14. Sweat gland carcinoma of skin (not of brea[illegible] To show the infiltration of carcinoma cells among smoot[illegible] muscle fibers which frequently surround sweat gland t[illegible]ules.

shown by Sir Astley Cooper who studied the secretion of sweat in the skin of the breast after death. "If the breast is wiped dry then compressed, it will continue to perspire after being dried several times. This is observed more especially if the cuticle has been separated by putrefaction."

The mammary gland was formerly thought to be the homologue of sebaceous glands and the production of milk a process analogous to the activity of the latter. Gegenbauer even assumed a diphlectic origin of the breasts in different species. He believed that the breast in certain of the lower animals developed from primitive tubular glands of the sweat gland type; whereas the breasts in other animals, above the Monotremata in evolution, have acinous, lobular structure finding homology in the sebaceous glands. This theory is unsound and not substantiated by our studies. The secretion of the sebaceous glands entails a destruction or decomposition of the gland cell called by Virchow "necrobiosis." The lactating mammary glands never show stratification and subsequent destruction of the secretory cells, which further disproves this theory, Kolliker and Virchow to the contrary. The manner in which the sweat gland secretes is not thoroughly known, but there is sufficient evidence at hand to warrant the conclusion by anatomists and physiologists, that secretion occurs by the separation of soluble chemical substances from the cells. The nuclei of the cells become pigmented and fat accumulates in the cystoplasm and is therein transformed into secretion. The process of secretion does not entail any destruction or even substantial changes in the sweat gland cell. Heidenhain found the breast to secrete in a similar manner except that it has differentiated to such an extent that it can secrete fat. Functionally, both the sweat glands of the skin and the breast are merocrine glands in that they are secreting epithelial cells and do not undergo necrobiosis. The breast may, therefore, be defined as a modified sweat gland of the skin secreting milk, the unique component of this secretion being fat.

APOCRINE AND EXOCRINE SWEAT GLANDS—THE BREAST AS AN APOCRINE SWEAT GLAND

There are two different types of sweat glands in the skin. The numerous small sweat glands with terminal coiled tubules, which are widely distributed over the entire body and are particularly frequent on the palms, soles, and face are termed exocrine sweat glands. Departures from the usual structure of these sudoriparous glands occur in certain regions of the body. If we except the eyelids with their specialized sweat glands (of Moll), these locations are the mammary and axillary regions, the scrotum, the inguinal folds, the labia majora, and the anus. According to Robin, certain parts of the side of the face contain these glands, where they are mixed

with the other sweat glands in the proportion of 1 to 10. According to Sappey in the first edition of his treatise on anatomy, these large sweat glands may range widely over the lateral and anterior thoracic walls. These latter sweat glands, known as apocrine glands, differ markedly from the common sweat glands of the skin. They are relatively very large and their tubules have secondary ramifying ducts similar to the racemose arrangement of the mammary gland. The inner secretory epithelium of the apocrine sweat glands is composed of dilated columnar cells, with eosinophilic cytoplasm and a tendency to papillary formation. They are histologically similar to the sweat gland tubules found in the breast; therefore, it is assumed that the breast originates from the apocrine type of sweat gland.

The fundus of the small exocrine sweat glands is a smooth coiled tubule with a narrow lumen, whereas the apocrine sweat glands of the axilla are made up of racemose tubules that evaginate forming wide saccules.

The exocrine glands, which carry the major burden of the secretion of sweat and the regulation of the body temperature, are highly functional in children. The apocrine sweat glands are closely related to the sex glands and their development is largely in abeyance until puberty is reached. In the female, the apocrine glands of the axilla begin to enlarge in the ninth year but in the male they do not take on their secondary growth activity until the time of puberty (Luneberg, 1902). These axillary sweat glands occur in the midst of great numbers of small exocrine sweat glands. The apocrine glands are composed of an inner layer of high eosinophilic secreting cells and an outer single layer of myo-epithelial cells.

As further proof of their relation to the sex glands, in common with the breast, it is of interest to know that the apocrine sweat glands are stimulated or depressed according to the various stages of the menstrual cycle. Not only do these apocrine glands become more prominent at puberty in common with the breasts and other genital apparatus, but they undergo enormous hypertrophy during pregnancy along with the breast and uterus and other genital structures. The secretory activity of the axillary sweat glands increases

Tail of Breast. 8 cases 11 %
Upper Outer. 23 cases 33 %
Upper Inner. 3 cases 4 %
Central 12 Cases 17 %
Lower Outer. 11 cases 15 %
Lower Inner 4 cases. 6 %
Entire Breast. 3 cases (4%).
Bilateral Involvement. 3 cases (4%)
Fold of Breast. 7 cases 10 %

Fig. 15. The regional distribution of sweat gland carcinomata of the breast. Note the preponderance in the margins and tail of the breast.

during the lactational period. The secretory activity of the axillary apocrine sweat glands regresses within a fortnight after the cessation of nursing and the loss of stimulation induced by suckling. The apocrine sweat glands of the axilla in humans occur in greatest abundance in a definite patch in the apex of the armpit usually not more than an inch in diameter and one-tenth of an inch thick. The enlargement of these axillary apocrine glands during pregnancy may reach the size of a hen's egg and they may be erroneously diagnosed as aberrant breast tissue or polymastia. This diagnosis is made the more readily because they may secrete a thin opalescent fluid which contains colostrum corpuscles. The difference between these functioning hypertrophied apocrine sweat glands during pregnancy and the slightly more developed aberrant breast tissue in the axilla is very slight from the standpoint of histogenesis. The secretion from the axillary and

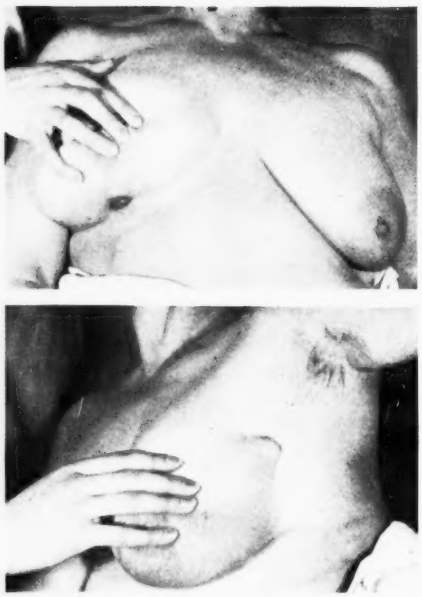

Fig. 16. Primary bilateral sweat gland carcinomata of the breasts in the same patient. In the right breast, the tumor is situated in the submammary fold, in the left breast the tumor is located in the axillary tail, both common sites of predilection for sweat gland cancers. Note the early marked attachment to skin.

inguinal apocrine glands, even in normal conditions, is different from sweat in other parts of the body. Another argument substantiating the relationship of these glands to the sex glands in common with the breast, is the fact that the odor from these particular sweat glands provokes sexual stimulation in certain of the lower animals.

Apocrine sweat gland cysts of the axilla occur occasionally. Primary adenocarcinomata may occur in these cysts. The possibility exists that some of the primary cancers in aberrant breast tissue in the axilla may originate in apocrine sweat gland structures. Tiny sweat gland adenomata are often found in the skin of the scrotum and penis.

COMPARATIVE ANATOMY OF THE BREAST, PHYLOGENETIC RELATION TO SWEAT GLANDS

The order of mammalia takes its name from these specialized cutaneous glands or mammæ. The character and complexity of the breast

Fig. 17. Superficial ulcerating sweat gland carcinoma of the breast. The location and ulceration of this lesion are characteristic of but not peculiar to sweat gland carcinomata.

changes markedly from the primitive tubular glands of the lower orders of mammals to the human breast, yet the fundamental structure and function remain essentially the same.

In the Echidna, which are Monotremata and the lowest order of mammals, there are no sweat glands on the entire body except a few in the immediate vicinity of the breasts. This remarkable anatomical fact strongly suggests that these surplus sweat glands are genetically related to the mammary glands in this animal. The deposit of large sweat glands under the areola in man is very likely a by-product in the evolution of the breast from these primitive types. The opposite condition obtains in the ornithorhynchi, where the mammary organs have appropriated actually all of the sweat glands on the ventral body surface. In certain of the plated animals, the breasts are not developed as isolated discrete organs, but the secretion of a milk-like pabulum occurs over the major portion of the body surface and the young obtain their nourishment, not by suckling, but by licking this sticky secretion as it appears. In the cetacea, large muscle walled sweat glands of the apocrine type are found near the mammary slits and on the vulva, although they occur nowhere else in the cetacean skin.

The excretory cutaneous glands of amphibia (e.g., frogs) are of the same two varieties as found in human skin, a common small gland secreting a clear watery or mucinous product, and a larger specialized kind, occurring only

Fig. 18.

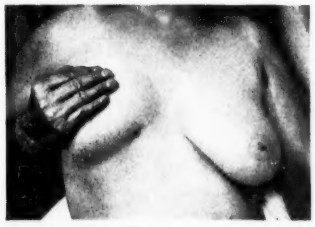

Fig. 19.

Fig. 20.

Fig. 18. Primary inoperable sweat gland carcinoma of axillary tail of breast.

Fig. 19. Early sweat gland carcinoma of the submammary fold, verified by microscopic examination. The clinical features of this lesion closely simulated traumatic fat necrosis of the breast, which is also of frequent occurrence in this region.

Fig. 20. Sweat gland carcinoma of the submammary fold of the breast, which is infiltrating and ulcerating the skin.

in certain regions of the body and secreting and opaque white substance, the analogue of true milk. The thumb gland, which occurs only in the male frog, has a functional and structural resemblance to the apocrine sweat glands. This thumb gland is a true sexual organ and enlarges considerably during the breeding season. It is a racemose tubular gland with a myo-epithelial cell layer, similar in every respect to the apocrine glands of the human groin and axilla.

The breasts of marsupials, such as the kangaroo, are within a ventral pouch which harbors the immature fetuses. At the time these tiny immature fetuses attach themselves immovably to the nipples which nourish them, the secretion of the breast is mucinous and the structure is primitive; as the young develop, the breast and its secretion undergo corresponding modifications, so that its structure is more complex (i.e., acinous rather than tubular) and the lacteal fluid approaches the composition of milk. It may be said therefore that the breast of the kangaroo during a single lactational period, exhibits the various evolutionary changes seen in all the species of mammals, from the simple primitive gland of the sudoriparous type to the complex organ, characteristic of the higher vertebrates.

Moles are said to have few sweat glands of either kind, while the closely related shrews have a great sexual development of the large apocrine glands along the flanks. Creighton has called attention to certain accessory sexual glands in the hippopotamus, which secrete the so called "bloody-sweat" of that species. This fluid is a glairy substance, the color of diluted port wine. The glands which secrete this liquid are branching tubular apocrine glands, situated on certain parts of the dorsal surface of this animal. They are not accessory breasts but are phylogenetically related to the breasts.

Creighton has given a good conclusion, which we shall quote in part: "The true milk gland of the higher classes retains traces of its descent from sweat glands, found either in the convolute tubular type of its rudiment and the muscular basement of its ducts, or failing the latter, in a basal layer of epithelial cells in the ducts. The muscle cells are very prominent in the more primitive types, but with the development of acinous lobules this muscular element tends to be lost. What really distinguishes the human breast from the monotreme mamma (and the still more primitive sweat glands) is the acquisition or addition of acinous lobules in which the milk is secreted. The foundation of original tubules is retained for ducts."

SWEAT GLAND CYSTS AND ADENOMATA OF THE BREAST

Our knowledge of sweat gland structures in the breast and their histogenetic significance has been obtained largely through microscopical study of cystic diseases of the breast. The majority of investigators have studied "sweat gland cysts" rather than

Fig. 21. Ulcerating sweat gland carcinoma of the submammary fold of the breast. Figures 19, 20, and 21 illustrate different stages in development of the sweat gland cancers of this region.

Fig. 22. Recurrent inoperable sweat gland carcinoma of right breast. The entire breast is involved by a diffusely infiltrating duct carcinoma. Once the sweat gland carcinoma is fully established, its local and systemic behavior is similar in almost every respect to the more common cancers of the lacteal gland.

"sweat gland carcinomata"; on this account we shall give a detailed historical résumé of their researches.

The names of three men in particular, are associated indelibly with the theory of sweat gland cysts and sweat gland carcinomata of the breast: Krompecher, in Germany; Creighton, in England; and Ewing, in the United States. The latter has had great experience with these sweat gland cancers; it has been our privilege to review his abundant material. Mansell Moullin, in 1881, described pea sized cysts in the mammary gland, which were surrounded by parallel hoop-like rows of spindle cells. Although not identified as such, these cysts filled all the histological requirements of sweat gland origin. This is the first report we have been able to find in the literature wherein these peculiar structures were recognized. Juengst, in 1884, described similar cysts accompanying an intracanalicular myxoma of the breast. It remained, however, for Krompecher, in 1897, to identify these cystic structures as sweat gland cysts and to formulate the theory of histogenesis of sweat gland tumors. Dawson erroneously ascribes this original discovery to Borst, who, in 1904, demonstrated some mammary fibroadenomata, which in circumscribed places showed large, irregular, pale, cylindrical cells with compact homogeneous cytoplasm and nuclei of different size. These polymorphous high cylindrical cells with occasional giant nuclei were often arranged in stratified arcade-like columnar epithelium. Von Saar, in 1907, reported two mammary cysts lined with large cells, containing a bright red, fine grained protoplasm; the cells never formed true vessel-bearing papillæ although they were stratified in papillary tufts. Von Saar designated these cells as "pale epithelium" to distinguish them from the basophilic cells of the lacteal epithelium. Billroth found these peculiar cysts most commonly on the extreme periphery of the breast, from which he inferred that a lobule here or there had failed to develop normally.

Krompecher's researches deserve a thorough summary. The cystic disease of the breast variously known as the *maladie kystique* (Reclus), cystadenoma (Schimmelbusch), and *mastitis chronica cystica* (Koenig) is neither a tumor nor an inflammatory lesion according to Krompecher, but it is an anomaly of the mammary gland, consisting of small cysts analogous to sweat gland cysts. This author designates this disease as hydrocystoma mammæ multiplex and points out its morphological correspondence to the cysts of the axillary sweat glands. The first beginnings of this so called hydrocystoma of the breast consisting of such typical sweat gland cysts lined with pale epithelial cells and appearing grossly as bluish or greenish transparent vesicles from a millimeter to a centimeter in size, are not infrequently found, as Krompecher observed, at autopsies in apparently normal female breasts. He found them in well developed as well as in involuted breasts and occasionally in adolescents. Even the male is not exempt from this disease, as Krompecher has reported a typical case of sweat gland

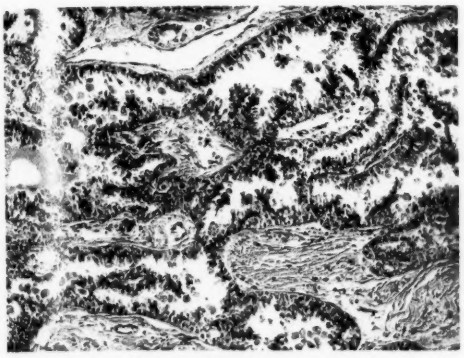

Fig. 23. Papillary cystadenocarcinoma of breast sweat gland type. Low grade of malignancy (grade one plus or two minus) because of the degree of differentiation. It is quite radiosensitive; its vulnerability is attributed to the character of the stroma rather than to the carcinoma cells *per se*. The tumor is mostly intracystic and intraductal.

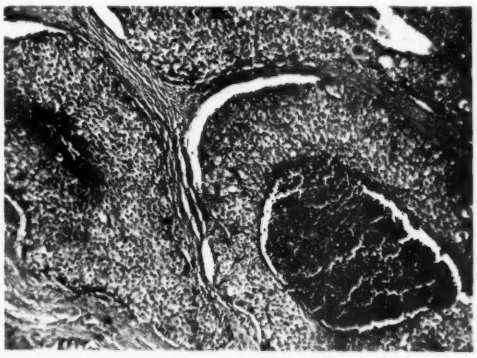

Fig. 24. Duct carcinoma ("comedo"-carcinoma) of sweat gland type. This histological variety of cancer is frequently found in lacteal ducts as well as in sweat gland ducts. In the latter case the ducts are gigantic and the carcinoma cells are larger and more conspicuously eosinophilic than in the lacteal duct cancers.

cyst of the breast in a male subject. The minute histological description of the cysts as given by Krompecher agrees in every particular with our own microscopical studies. The considerable size of the cells, the knob-like or clubbed protuberances of the cylindrical epithelium, the abundant compact, homogeneous, pale, eosinophilic cystoplasm and the small, round, and occasionally giant nuclei comprise a characteristic microscopical picture. The peculiar pale epithelium of the cysts and tubules is very sharply differentiated from the lacteal epithelium and the excretory ducts of the breast. The cell boundaries are frequently indistinct and the adjacent cells in such cases appear to be confluent, forming giant polynuclear cells. Krompecher noted (and we have many times confirmed this observation) that the sweat gland epithelium in the breast is especially inclined to proliferate and form papillæ. The majority of the papillary cystadenomata of the mammary gland originate from lacteal epithelium, but there are many others of the sweat gland type (Fig. 6). Krompecher found this pale sweat gland epithelium as the basic structure in 21 cysts, 12 benign fibro-adenomata, and 9 cancers in the group of 292 benign and malignant breast tumors comprising his material. In only 3 of the cancers, however, was he able to demonstrate the characteristic long spindle cells running in parallel groups around the basement membranes.

Kuru observed this "pale epithelium" in 3 breast tumors and emphasized the relative smallness of the nuclei. Von Saar likewise referred to the close similarity of the mammary cysts to the sweat glands, in which the resemblance extends to the fine details of histological structure. Although we have emphasized the occurrence of sweat gland cysts in the microcystic variety of Reclus' disease (non-inflammatory fibrosis) we do not mean to infer that they are pathognomonic for this disease because the majority of the cystic structures are lined by ordinary lacteal epithelium.

The specificity of sweat gland cysts in the breast is generally recognized by the French school. Roussy states, in his recent textbook on cancer, that there is normally a mixture of two kinds of glandular tissues in the breast: one, the acinar glandular groups of the lacteal type, and another of ramified ducts of the sudoriparous type, lined by tall pyriform eosinophilic cells and occurring commonly in the axillary region. Letulle terms these sweat gland cysts of the breast "idrosadenoides."

Our youngest patient with sweat gland cysts of the breast was 26 years of age. Herzenberg found numerous pea-sized red nodules in both breasts of a stillborn infant.

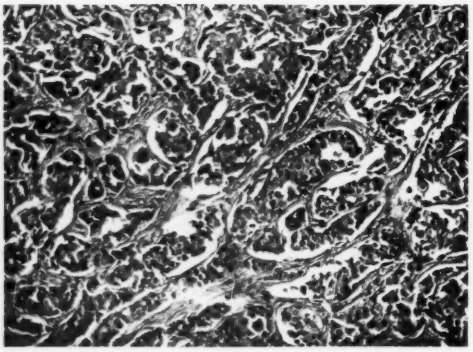

Fig. 25. Infiltrating sweat gland carcinoma of the breast. Typical structure of many of these cancers. Marked eosinophilia.

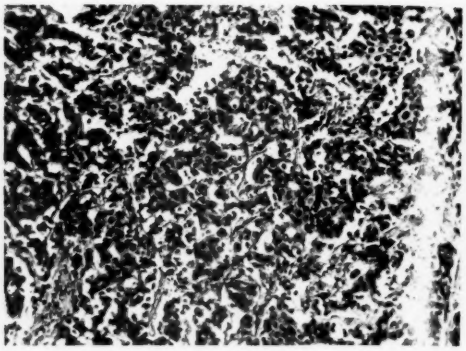

Fig. 26. Infiltrating papillary adenocarcinoma of the breast of the sweat gland type. Grade two plus. Radiosensitive.

The nodules when examined microscopically proved to be cystic apocrine sweat glands.

We have seen sweat gland cysts and lacteal cysts immediately adjacent to each other and in several instances have been able by serial sections to trace these cysts and tubules to the point of anastomosis with lacteal ducts. Cheatle likewise states that in serial section he has always been able to trace these cysts of the sweat gland type into the ducts of the breast. Semb found the pale and normal epithelium merging directly into each other in the same cystic duct of the breast. Although this may occur, it is unusual; more commonly an entire branch of a duct and its ramifications are completely involved in the process.

Presumably the factors predisposing to sweat gland cysts are the same as in lacteal cysts of the breast. Similar cysts have been produced experimentally in extramammary sweat glands; these cysts are microscopically identical with the so called sweat gland cysts of the breast. The experiments of Schidachi were successful in producing cysts of this type. He made semicircular linear incisions through the skin of the paws of narcotized cats, about the level of the excretory ducts of the sweat glands and parallel to the surface of the epidermis. The partially severed discs were then sutured back onto the paws, the cats were given pilocarpine solution to stimulate the secretion of sweat and 3 to 9 weeks later were killed. On microscopical examination hydrocysts of the sweat glands had originated directly from the excretory ducts and resembled in every respect the sweat gland cysts found in humans, especially in the axilla and breasts.

In a recent article, Dawson vigorously attacks the hypothesis that these structures are of sweat gland origin. He asserts that the pale epithelium commonly identified as sweat gland epithelium is not related at any stage with sweat gland tissue and that it occurs in the breast too frequently to warrant the supposition of accidental inclusion as a developmental anomaly. He observed these cells in 120 breasts with malignant tumors and in 48 breasts with benign cysts all of which had the entire breast minutely examined microscopically in whole breast sections. We quote one of his arguments as follows: "An important and essential point to note is that in all cases this pale epithelium in the breast lines a definitely cystic structure, although the size of the cysts may vary within wide limits. Even the smallest pale structures are always larger than normal mammary acini." Dawson's assertion that these pale structures are found invariably associated with the formation of cysts in the breast is not substantiated by our studies (Figs. 5, 8, frontispiece, 9). This difference in size, although a distinguishing feature does not necessarily indicate that the so called sweat gland tubules are cystic and degenerated as compared with the smaller lacteal tubules. In the human

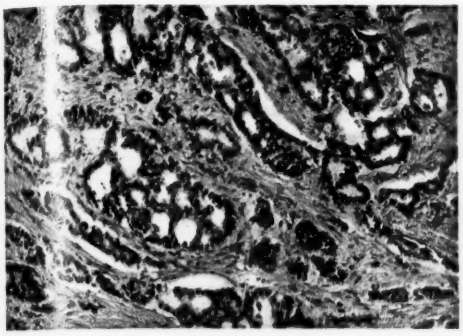

Fig. 27. See clinical photograph, Figure 21. Alveolar sweat gland carcinoma of breast. Grade two. Moderately malignant. Some papillary structure.

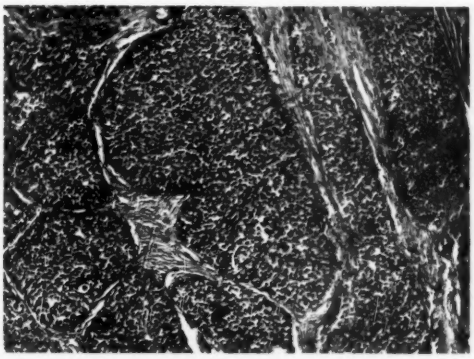

Fig. 28. Medullary sweat gland carcinoma of breast. Grade two plus. With increasing anaplasia, the cells tend to lose their eosinophilia; this change is more apparent than real because the nuclei are larger, the cell bodies are smaller, and eosinophilic cytoplasm is less conspicuous.

breast the lacteal tubules are largely excretory ducts and their lining epithelium is not highly functional, whereas the primitive tubules, such as the sweat gland structures are assumed to be, are lined by high columnar secretory cells. An analogy exists in the case of the developing kidney. The secretory units of the primitive kidney become the collecting tubules of the mammalian kidney, and are morphologically quite different from secretory units such as the convoluted tubules. The sweat gland tubules have not differentiated sufficiently to be anatomically and functionally similar to the lacteal epithelium.

It is true that cell degeneration with the formation of cysts is more common in sweat gland structures in the breast than in the other mammary tissues. This is frequently the case in embryonal anomalies and should not be considered as evidence that all these sweat gland structures are degenerative. Many sweat gland cysts contain cell detritus made up of the desquamated pale epithelium.

Dawson presents another argument for the degenerative theory by calling attention to the fact that pale eosinophilic glandular epithelium has been observed in the ovary, uterus, prostate, and kidney, all of which are the site of possible cystic degeneration. Dawson furthermore states: "The onset of the pale change is post-proliferative and an evidence of a checked and receding epithelial activity." We have previously stated that sweat gland cysts and tubules are characteristically prone to form papillary ingrowths, yet we have never seen these structures prior to the supposed change wherein the epithelium becomes eosinophilic. If Dawson's observations are true we should see this many layered proliferating epithelium before it degenerates and becomes eosinophilic. Furthermore, all stages of the transition should be visible and we would not expect to see the uniformity in structure which the sweat gland tubules and cysts constantly show in serial section. It is our belief, therefore, that the eosinophilia and other anatomical characteristics of these cells, precede and accompany the proliferative changes.

There are numerous other theories extant to explain the presence of these structures in the mammary gland. McFarland has considered them to be residual (i.e., non-involuted) lactation acini, although many pathologists have discovered them in non-lactating, virginal, and even infant breasts. Prym considers the pale epithelium as metaplastic mature breast tissue predominantly acinar tissue.

SWEAT GLAND CARCINOMA OF THE BREAST

Krompecher was the first to observe the cancerous transformation of the pale epithelium characteristic of sweat gland tubules and cysts. He commented on the active participation of the pale epithelial cells of these cysts and the intracanalicular cystadenomata in

the carcinomatous proliferations. The eosinophilic cells form stratified layers and papillæ within the cysts, occasionally even blocking the lumina and forming pale epithelial nests and alveoli. According to this author, these relations demonstrate that both intracanalicular cystadenomata and true carcinomata can originate directly from the pale epithelium of the sweat gland cysts.

Berka studied the intracystic papillary formations in sweat gland cysts and considered the process as something intermediate between metaplasia and anaplasia. Furthermore, he noted a close resemblance of these large pale eosinophilic cells to certain atypical elements in large cell carcinomata of the breast, without, however, showing definite malignant growth. Charteris studied whole sections of 48 breasts removed for carcinoma. He saw these pale cells of the sweat gland type and even noted the development of carcinoma from them.

Other pathologists are definitely opposed to the theory that these sweat gland cysts with intracystic proliferations are precancerous and even deny that carcinoma ever developed from this pale epithelium. Von Saar in particular states that no direct transformation of these cells into carcinoma has ever been confirmed.

Dawson calls attention to the rarity of sweat gland carcinoma of the skin; he found only one specimen of this type in 13,500 pathological lesions studied. Because of this fact, he cannot understand why the malignant possibilities of these so called sweat gland structures should be so much enhanced when they supposedly form a normal inclusion in the breast substance. Contrary to this view, it is our opinion that sweat gland ducts and cysts in the human breast should be even more prone to undergo malignant degeneration because of the well known tendency of aberrant primitive and embryonal structures to become malignant.

Dawson has classified the conflicting opinions concerning the nature and possibilities of the "pale epithelium" into two definite groups, namely: (a) "The pale epithelium indicates a proliferative change, with a more or less definite possibility of later malignant development." (Krompecher, Borst, Ewing, Cheatle and Cutler, Creighton). (b) "The pale epithelium indicates a proliferative change with later, and progressive, degeneration." (Von Saar, Theile, Deaver and McFarland, Bloodgood, Prym).

Although Theile once observed an actual transition from pale epithelium to carcinoma, he states that he found in the pale epithelium no specific kind of cell, "but only a degeneration form, originating under certain external conditions, which are distinguished from the normal gland cells by a stronger growth energy (formation of epithelial papillæ) and secretory activity (vacuoles) or even by a briefer period of life." We cannot comprehend how a cell can exhibit "stronger growth energy" when it is degenerating. It seems more likely that the eosinophilic character and the large size of the pale cells are characteristic of the sweat gland epithelium in as much as they persist in the majority of cases after malignant change has supervened. In Cheatle and Cutler's experience, this peculiar staining property of the pale cell disappears when the neoplastic stage is manifested. A study of our material shows that this change occurs especially when the carcinoma becomes increasingly malignant and exhibits anaplastic tendencies. Thus we have several specimens in which a fairly well differentiated sweat gland carcinoma has the large pale eosinophilic cells in certain regions, while in other portions of the same carcinoma, the cells are smaller, more hyperchromatic, less differentiated, and presumably more malignant.

It is our opinion that the sweat gland features of these structures in the mammary gland may be found in all pathological stages, from the normal breast, microcystic disease of the breast, benign tumors, and precancerous intraductal papillomatous processes, to carcinoma. A recent specimen in our collection exhibits all of these stages in sweat gland cysts, an intraductal papillary cystadenoma, and a true sweat gland carcinoma. It is unlikely that the cysts, the intraductal cystadenoma, and the carcinoma have all undergone degeneration simultaneously and uniformly throughout. Mitotic figures found in the eosinophilic sweat gland cells verify their active participation in cell multiplication and

the growth of the carcinoma. Dawson maintains that these mitotic figures represent "agonal mitoses" in dying cells.

The first detailed and accurate description of the growth and microscopic pathology of sweat gland carcinoma of the breast was reported by Ewing. This author states that a considerable proportion of mammary cancers arise in sweat glands of the breast; in his material, this proportion is in the neighborhood of 25 per cent. We have recently analyzed a group of 166 histologically verified primary operable carcinomata of the breast and in this group 41, or practically 25 per cent, were of the sweat gland type. The sweat gland cancers of the breast may be either cystic or solid. Aside from their peculiar distribution in the breast there are few distinguishing features of this type of mammary cancer except that they are usually more yellow than other mammary carcinomata. Ewing attributes this yellow color to xanthomatous changes which are more frequent in sweat gland cancers than in other varieties.

Our material is the same from which Ewing made his original observations. He found that the majority of the papillary cystadenocarcinomata and the glandular adenocarcinomata with cuboidal clear cells and basophilic cytoplasm develop from the lacteal ducts, whereas the sweat gland ducts of the breast give rise chiefly to papillary and adenocarcinomata in which the cells are columnar rather than cuboidal. These cells are predominantly eosinophilic. Some of the comedo carcinomata or duct carcinomata are of this type although in such cancers the ducts are usually much larger than in the case of carcinoma of the lacteal ducts. The tendency of the sweat gland carcinomata to form papillary structures is in keeping with this same inclination of the sweat gland cysts and tubules.

The eosinophilia of the cytoplasm in the well differentiated sweat gland carcinomata testifies to the sudoriparous origin of these cells, which is further emphasized by the presence of certain cells of the myo-epithelial type arranged in a comb-like fashion at the periphery of the neoplastic nodules. These cells are found only rarely and then only in those cancers which are not invasive and do not destroy the integrity of the surrounding breast tissue. The myo-epithelial cells are either not reproduced in the rapid growing sweat gland carcinomata, or if they are present, they are not recognized as such.

Some of the sweat gland carcinomata in our collection are made up of clusters of large alveoli lined with one or occasionally two rows of opaque eosinophilic cells with supporting cells lying on a well defined basement membrane. The morphological and staining characteristics which distinguish them from other carcinomata of the breast may be lost in the anaplastic varieties; this is quite evident in studying the metastases from such cancers. Except for these properties which we have enumerated, the sweat gland carcinomata of the breast have much the same structure as other mammary cancers; indeed, we find that the bulky adenocarcinomata, the comedocarcinomata, the papillary intraductal and intracystic adenocarcinomata, the medullary carcinomata, the carcinoma simplex, and even scirrhous carcinomata of the breast, are represented in this group although the distribution is not the same as in the case of carcinomata arising from the lacteal ducts.

We have shown in our clinical analysis of 81 cases of sweat gland carcinomata of the breast that this tumor is more frequently adherent to the skin than is the ordinary breast cancer. Pain occurs in only 8 per cent of the general group of mammary cancers, whereas in the sweat gland carcinomata of the breast, it is the predominant symptom in 34 per cent of the patients. Approximately two-thirds of these carcinomata were situated in the periphery of the breast, where the apocrine sweat glands are most abundant. We sometimes find these sweat gland carcinomata in the subareolar region adjacent to the great ducts near the nipple.

CLINICAL REPORT OF EIGHTY-ONE SWEAT GLAND CANCERS OF THE BREAST

Age. The average age of 2,663 patients with mammary cancer who applied to the Memorial Hospital was 51 years; this same age was also the average for the 81 patients with sweat gland carcinoma of the breast. The oldest patient with any type of mammary

Age group	Carcinoma of the Breast		Sweat Gland Carcinoma of the Breast	
	Number	Per cent	Number	Per cent
Under 25	8	0.3	1	1.2
25 to 29	51	1.9	1	1.2
30 to 34	136	5.2	5	6.2
35 to 39	266	10.0	5	6.2
40 to 44	384	14.4	10	12.4
45 to 49	443	16.7	14	17.3
50 to 54	426	16.0	13	16.0
55 to 59	335	12.6	14	17.3
60 to 64	284	10.7	12	14.9
65 to 69	156	6.0	1	1.2
70 to 74	105	3.6	3	3.7
75 to 79	51	1.9	0	0.
80 to 84	13	0.5	2	2.4
84 to 94	5	0.2	0	0.
Totals	2663	100.0	81	100.0

cancer was 90 years and the youngest 17 years, while the eldest patient with sweat gland cancer of the breast was 84 years and the youngest 19 years of age. The diagnosis in both cases was "primary operable" carcinoma of the breast.

Race. The distribution of these patients according to racial origin is not particularly significant. There were 27 Americans, 14 Irish, 7 Hebrews, 6 Russians, 5 Negroes, 3 Germans, 2 Italians, 2 Newfoundlanders, 2 Polish, 1 Norwegian, 1 Swede, 1 Swiss, 1 Hungarian, and 1 Turkish patient. The complexion of 24 of these patients was recorded, of which 95 per cent were brunettes. Sweat gland cancers of the breast occur more frequently in women whose skins are oily and contain large pores, so we would expect a predominance in brunettes because of their coarser skin textures.

History of lactation. Data concerning lactation was available for 67 patients, of whom 60 per cent had nursed one or more children; of the 26 non-lactating breasts, 40 per cent were in single women. Seven patients (12 per cent) stated that the cancerous breast had been non-functional due either to abscess formation, caking, insufficient secretion, or to the fact that it was more convenient to nurse the baby on the other breast. Sixteen patients (20 per cent) had experienced one or more interrupted pregnancies. One woman had 4 full term pregnancies and 11 miscarriages. No conclusion can be drawn from this study concerning the influence of lactation in the production of sweat gland carcinoma.

Trauma. Twenty-two patients gave a definite history of trauma to the affected breast while 45 others asserted that they could recall no injury to their breasts. The character of the trauma varied; however 15 women, or 68 per cent of those with breast injuries, stated that a single blow was considered by them to be the cause of the cancer. One patient had sustained the trauma 12 years prior to the detection of the tumor, and 3 had discovered a tumor very shortly after the date of injury. The average time elapsing between the trauma and the recognition of the cancer was 2 years. We do not ascribe any etiological importance to the history of trauma recited by these patients, for 2 reasons; the interval of time was usually too great and the presence of preexisting tumors could not be ruled out in the 3 instances in which tumors appeared suddenly after injury. In our experience a single trauma has never caused cancer of the breast. We, therefore, believe these histories of single trauma to be of little or no significance. Two women attributed their cancers to chronic irritation by sharp corset steels; this condition was not unusual several years ago when high ribbed corsets were in vogue, as sweat gland cancers of the breast are frequently situated in the mammary fold. Although but 2 women gave histories of chronic irritation from ill-fitting corsets impinging on the lower margin of the breast, we believe this type of chronic irritation may not infrequently serve as an exciting cause of sweat gland carcinoma in the lower breast segment.

First symptom. In 77 cases the history contained a definite statement concerning the first symptom observed by the patient. Fifty-seven patients (76 per cent) gave the discovery of a lump in the breast as their first

symptom, and this parallels our experience in a survey of the first symptom in 1,000 cases of mammary carcinoma in general. Fifteen of these patients had inoperable cancers at the time of diagnosis. In 10 per cent of the cases, a discharge from the nipple preceded the discovery of the tumor as compared with 1.5 per cent in the survey previously mentioned. Eight per cent noticed pain as the first evidence of disease, either in the affected breast or in the arm and shoulder of the same side, which is the identical figure in the 1,000 breast cancers surveyed including all types. The 6 per cent remaining had miscellaneous first symptoms, such as an increase in the size of the breast, ulceration of the mammary skin, tumefaction of the nipple, or bulky axillary lymph nodes.

Size of tumor. Six of the primary operable carcinomata (14 per cent) were greater than 6 centimeters, 25 (57 per cent) were 3 to 6 centimeters in diameter, and 13 (29 per cent) were less than 3 centimeters in size. Of the primary inoperable carcinomata, 6 were greater than 6 centimeters in diameter, 8 measured 3 to 6 centimeters, and only 2 tumors were smaller than 3 centimeters in size. The operability of any particular sweat gland cancer was never determined by the measurements of the primary tumor, but we are recording them to afford complete clinical data.

Location. Dependable data concerning the location of the tumor is available in 74 cases of this series. The accompanying diagram (Fig. 15) shows the regional tumor sites in these patients. In one-sixth of all the cases the growth occurred in the central segment immediately beneath the areola. Eleven per cent of the sweat gland cancers were located in the axillary tail of the breast, 33 per cent in the upper outer quadrant, and 10 per cent in the submammary fold. This division is somewhat arbitrary as many tumors which are really located in the axillary extension of the breast, spoken of in this paper as the "tail," are recorded to be in the upper outer quadrant. It seems significant that slightly more than half of these tumors are situated in the upper outer quadrant and margins of the breast, which regions contain numerous large apocrine sweat glands.

Rate of growth. Prior to this study it was believed at the Memorial Hospital that sweat gland cancers of the breast were relatively less malignant than some of the other histological varieties, but this opinion was not confirmed by our analysis of the cases. For example, 50 per cent of these cancers grew with great rapidity, and the 2 oldest patients, aged 84 and 82 years, had rapidly growing tumors. The rate of growth in 31 per cent of the cases was moderately rapid. The youngest patient, aged 19 years, had a slow growing tumor as did 19 per cent of the entire group. Contrary to our observations on mammary cancers in general, the sweat gland carcinomata of the breast are apparently not of more rapid growth in young subjects.

Pain. Sensory disturbances varying from slight mastalgia to severe pain in the breast, often radiating to the shoulder and arm, were noted by 28 patients (34 per cent). Sixteen of these patients (or one-third of the primary operable groups) experienced pain before treatment was given. Similar sensory disturbances were found in 9 patients (48 per cent) with primary inoperable breast cancers of this type. In the general group of breast cancers studied at the Memorial Hospital, pain has never been a frequent symptom, occurring in only 8 per cent of primary operable cancers. We attribute the unusual frequency of pain in sweat gland cancers of the breast to early skin attachment and ulceration.

Skin adherence and nipple retraction. Thirty-three (71 per cent) of the primary operable sweat gland cancers of the breast were adherent to skin. The cause of this early and frequent skin attachment probably lies in the superficial location of these tumors. The nipple was retracted or fixed in only 50 per cent of the cases, due to the fact that so many of these tumors were situated at the margins of the breast, where they could not exert traction on the nipple. Six of the nipples in patients with tumors centrally located were deeply ulcerated.

Metastasis to lymph nodes. Thirty-two (64 per cent) of the patients with primary operable sweat gland cancers had metastases (proved histologically) in the axillary lymph nodes.

The primary tumor was situated in 40 per cent of these cases in the upper outer quadrant of the breast or the axillary tail. Ten patients (53 per cent) with primary inoperable sweat gland cancers had axillary metastases but not supraclavicular; in 6 other inoperable cases (32 per cent) both axillary and supraclavicular lymph nodes were involved. Fifty-eight per cent of the patients with recurrent sweat gland cancers of the breast had metastases in the supraclavicular lymph nodes, which is the usual experience with mammary carcinomata in general.

Metastasis to lungs and pleura. Thirty-seven per cent of these women with inoperable sweat gland cancers of the breast and 25 per cent of those with recurrent lesions had pulmonary metastases demonstrable on roentgenograms.

Metastasis to bone. Only 7 patients (8 per cent) presented definite evidence of metastasis to bone. One young woman under 40 years of age had pre-operative X-ray therapy, local excision of the tumor, interstitial irradiation by platinum filtered radon needles, and postoperative X-irradiation for an operable sweat gland cancer; she developed pulmonary and bone metastases 1 year later. This rapid extension of the disease to osseous structures parallels our experience with many young women similarly treated for other forms of mammary cancer. Another young patient came to the Memorial Hospital with widespread skeletel involvement but no local recurrence, 4 years after a radical mastectomy had been done. Another woman, aged 48 years, with a slowly growing operable carcinoma and axillary metastases, developed bony metastases and died only 6 months after a radical mastectomy. An aged woman of 84 years had a rapidly growing sweat gland cancer, which originated beneath the nipple and early became ulcerated. She had metastases to bone at the time of admission in spite of which she lived 4 years after local excision of the tumor and external irradiation with X-rays and radium element pack.

End-results. Of the 50 patients with sweat gland cancers of the breast, classified as "primary operable," 21 are dead, 20 are living, and 9 have been lost to our observation. The 9 who have been lost to observation, either returned to a foreign country or moved to a distant state; one was known to be well for 6½ years, and another for 5 years after treatment. Of those who died, the average length of life from onset of symptoms to death was 3⅓ years and the average length of life after the institution of treatment was 2⅓ years. Five patients lived less than a year after therapy was started, the shortest time being 2 months. Thirty-six of the patients having primary operable sweat gland cancers of the breast were treated prior to January, 1927. In this group, 5 have been lost to further observation and 16 (44 per cent) are alive and well 5 years or more after treatment. Twenty of these patients were treated prior to January, 1925, and 8, or 40 per cent, are living and well 7 years after treatment. Seven patients with primary operable cancers of this type were treated before January, 1920 (13 years ago), and 2 of these (28.5 per cent) are living, apparently cured of the disease, at this time. These percentage figures are slightly higher than the end-result percentages recently computed at the Memorial Hospital for primary operable mammary cancers of all histological types, viz., 5 year survival without evidence of disease in 217 patients treated by radical mastectomy with pre-operative and postoperative irradiation, 41 per cent; 7 years, 35 per cent; 10 years, 22 per cent. We may conclude from these comparative statistics that the degree of malignancy and prognosis following treatment is practically the same for sweat gland cancers of the breast as it is for the general group of mammary cancers. If a large group of sweat gland carcinomata of the breast could be surveyed with respect to end-results, the comparison would be more significant.

In the primary inoperable group consisting of 19 patients, 14 are dead, 4 are living, and 1 has been lost to observation. One of the patients who died went into shock immediately after a palliative operation and lived less than 48 hours. The average duration of life after the onset of the disease was 3½ years; 2 other patients in this series stated that a lump was felt in the breast 20 years before admission to the Memorial Hospital. The average duration

of life after the initiation of therapy in these inoperable cases was 21 months, the longest being 5 years, and the shortest 4 months. Our 4 patients who are now alive were first treated, 9 years, 2 years, 19 months, and 8 months ago. The one who has lived 9 years without a recurrence was 57 years old when first seen in November, 1922. She had a bulky, fungating sweat gland cancer with ulceration of the nipple and metastasis to axillary lymph nodes. A roentgenogram of the chest was reported to have shadows suggestive of carcinomatous metastases; however, there has been no change in this picture to date. She was treated by radical mastectomy following a pre-operative X-ray cycle.

There have been 12 patients with recurrent sweat gland cancers of the breast; 6 are dead and 6 are living. The average time from the onset of the primary disease until death was 4¼ years, and the average length of life after treatment of the recurrent lesion at the Memorial Hospital was 10 months. The time elapsing between the operative treatment of the primary tumor and the application at Memorial Hospital because of a recurrence averaged 18 months for the 12 patients, the shortest being 18 days and the longest 4 years.

SUMMARY

The human breast develops as a modified apocrine sweat gland. Apparent sweat gland tubules and cysts occur in the normal adult breast where they anastomose with the interlobular lacteal ducts. The characteristic features which distinguish the mammary sweat gland tubules from the lacteal ducts are: constant eosinophilia of the cytoplasm, an inner layer of high columnar cells, the occasional presence of myo-epithelial cells surrounding the tubules and the tendency to form intratubular and intracystic papillary tufts. The anatomical and staining characteristics of these cells persist through all the transitional phases of normal sweat gland tubules, cysts, intracystic papillomas, adenomas, and carcinomas.

Evidence is presented to substantiate the theory that sweat gland carcinomata of the breast may develop from pre-existing sweat gland tubules, cysts, and papillary adenomata. The various stages in this transition have been seen. Except for the peculiar properties of sweat gland structures in the breast which we have enumerated, the sweat gland carcinomata of the breast have much the same structure as other mammary cancers, e.g., we find that the bulky adenocarcinomata, the comedocarcinomata, the papillary, intraductal, and intracystic carcinomata, the medullary carcinomata, the carcinoma simplex, and even scirrhous carcinomata of the breast are represented in this group.

Sweat gland cancers of the breast occur more frequently in swarthy brunettes, whose skin has large pores and oily, coarse texture. Their regional distribution is mostly on the periphery of the breast, particularly in the axillary tail and submammary fold. The frequency of pain, skin adherence, and ulceration are significant clinical features of sweat gland cancer of the breast. The degree of malignancy and the prognosis following treatment is practically the same for sweat gland cancers of the breast as it is for the general group of mammary cancers.

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PEPTIC ULCERS ARTIFICIALLY PRODUCED IN THE HUMAN BEING

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CLINICAL and experimental observation has now made it evident that the presence of the gastric juice is an important factor in the production of gastric ulcers. If the juice is allowed to act upon the mucosa of the duodenum, ileum, or jejunum in an undiluted state an ulcer almost invariably develops. Such a condition may be seen around the islands of gastric mucosa occasionally found in a Meckel's diverticulum or in a gastric pouch experimentally made, and united with the intestines (1).

The fact that the gastric juice does not invariably lead to ulceration of the normal stomach or of the jejunum after gastro-enterostomy has been the subject of prolonged investigation. One of the factors of importance is believed to be the dilution of the gastric juice which usually occurs in the stomach. Removal of the salivary glands (3) or the formation of an œsophagostomy opening through which all the saliva escapes is not invariably followed by ulceration nor does such regularly occur in patients with a complete œsophageal obstruction.

Matthews and Dragstedt also failed to produce ulceration in dogs after the performance of a gastrostomy and an œsophageal fistula whereby sham feeding was carried out and the secretion of acid was induced without being diluted by the food, which escaped through the fistula. If however, the alkaline secretion of the bile and pancreatic juice was removed, ulceration occurred in a high percentage of cases. Removal of these alkaline secretions was easily accomplished by excising the pylorus, closing the duodenal stump, dividing the jejunum just below the duodenojejunal flexure, anastomosing the cut end of the stomach with the distal end of the jejunum and the proximal end of the jejunum into the ileum close to the ileocæcal valve. Similar operations and results were performed by Mann (1).

These experiments were to a certain extent vitiated by the fact that the animal developed a cachexia and then died, probably owing to the effect of transposing two such important digestive secretions so low down in the ileum. When bile and pancreatic fluid were allowed to enter the intestines higher up, ulceration was less common. Matthews and Dragstedt have shown that this is probably due to regurgitation of the alkaline secretions for if regurgitation was prevented by an ingenious method they devised, the ulceration became more common.

The artificial formation of a pancreatic fistula which can be performed upon an animal kept alive by daily injections of salt solution is also followed by chronic ulceration. The important factor therefore in preventing the gastric juice producing an ulcer in a normal animal is the neutralizing effect of the pancreatic juice and bile.

The effect of such factors are much more difficult to determine in the human being. Although gastro-enterostomy is usually performed for chronic ulceration, in which the acid is usually high, gastrojejunal ulceration does not, in the hands of most surgeons, occur more frequently than in 3 per cent of the cases. In my own series of 1,247 gastro-enterostomies, such ulceration occurred in 25, that is 2 per cent. Moreover, after an adequately performed partial gastrectomy, my own experience agrees with that of Lord Moynihan, that such ulceration is practically unknown. In my own series of 466 partial gastrectomies it occurred in only one case in which it was known that gathe stric resection was insufficient.

In the human being the conditions experimentally produced in animals rarely occur, but it is interesting to note that the Roux operation of partial gastrectomy which most closely produced these conditions, in that the pancreatic juices entered the jejunum well below the end-to-side anastomosis, has now been universally abandoned as it was followed by so high a percentage of gastrojejunal ulceration. In the 2 following cases the

conditions experimentally produced in animals, were somewhat closely simulated and the resulting formation of chronic ulceration becomes of considerable clinical interest.

CASE 1. Development of peptic ulcer after partial pancreatectomy and partial gastrectomy.

A.E.L., male, aged 38 years, had suffered with attacks of epigastric pain from 1906 until 1913. The attacks would last for about 2 months and for 1 year they had been getting longer. The pain came on shortly after food, was severe in nature and often indeed agonizing. It was associated with vomiting which gave some relief to the pain. On June 23, 1913, he was operated upon by another surgeon who found what he thought to be a large carcinomatous ulcer in the middle of the stomach. In performing a partial gastrectomy, the surgeon realized that the neck of the pancreas had been cut through and practically the whole of the body removed with the ulcer. Pathological investigation showed that the ulcer was benign. This operation was apparently followed by the formation of a subphrenic abscess which was drained and the patient then steadily improved and put on weight. In 1916, however, his symptoms began to return. He then had attacks of radiating pain through the epigastrium to the lower abdomen. The pain occurred relatively late after food and was relieved by food. It was associated with vomiting which also gave considerable relief. In June, 1921, he was admitted to Hospital and his test meal showed free hydrochloric acid .15 per cent and a total acidity of 53. An X-ray investigation was performed and was said to be suggestive of a jejunal ulcer. He was treated by dieting. In September, 1922, he sought my advice as his symptoms had been getting worse. The pain would now wake him at night and the last attack had persisted for 6 weeks. His appetite had been getting poor and he had been losing weight. On examination there was some tenderness in the epigastrium but no definite tumour. His hydrochloric acid was now .12 per cent and his total acidity 45. The X-ray examination showed a constant meniscus in the region of the gastrojejunal opening. An operation was performed on September 20, 1922 and a gastrectomy of the Billroth II type was found. In the center of the anastomosis was a very large indurated ulcer. Practically no pancreatic tissue could be found. A more extensive partial gastrectomy was performed, only about half an inch of the lesser curvature being left. The excision was planned not only to remove a large portion of the stomach but also the loop of the jejunum attached to it. An anastomosis was carried out between the cut end of the stomach and the two cut ends of the jejunum by the Pólya method, the afferent loop being brought to the lesser curvature and the efferent to the greater curvature. The pathological report stated that there was a chronic progressive peptic ulcer in the jejunum and very numerous oxyntic cells in the gastric mucous membrane. The patient made an uninterrupted recovery and has been seen at frequent intervals in my follow-up department since. He is now quite free of symptoms, is taking all food and is able to live a perfectly normal life.

CASE 2. Development of peptic ulcer after cholecystenterostomy for pancreatitis.

J.G., male, aged 52 years, was first seen on July 9, 1929. For 4 months he had noticed that he was becoming jaundiced and had had some shivering attacks. For some 3 months there had been itching of the skin of the whole body which was relieved only by soda baths. His appetite had remained good, and there had been no pain of any sort. In spite of a careful diet and medical treatment, his jaundice had been progressing. He had lost a stone in weight in the last few months. On examination he was found to be a thin, jaundiced, restless man. The liver could be felt uniformly and smoothly enlarged. There was no tenderness. The gall bladder could not be felt. The stools were clay colored. An operation was performed on July 12. The pancreas was found to be uniformly hard and enlarged, and there were no localized nodules. The head and body presented a similar consistency. The gall bladder was distended and tense but tucked away under the enlarged liver. There was no evidence of any secondary growths and no stone or growth could be felt in the common bile duct. The stomach was smooth and the duodenum was tied down in the right lumbar region. It was found that the gall bladder could only be approximated to the duodenum or stomach with some difficulty and it was, therefore, thought wiser to bring a loop of small intestine about 18 inches from the duodenojejunal flexure up through the mesocolon. The gall bladder was emptied, and thick, tenacious bile was removed and an anastomosis was then performed between it and the loop of the small intestine. The patient made very good progress and his jaundice rapidly decreased. Three months later he was feeling very well. On January 24, 1930, he complained of having had indigestion for 2 weeks and on March 18, he was found to be very anæmic and complained of epigastric pain passing to the back. This was severe and occurred late after food. He was admitted to hospital and the stools were found to be very black and contained a large amount of blood. There was a considerable degree of anæmia. The test meal showed free hydrochloric acid .16 per cent and a total acidity of 75. An X-ray investigation showed a clear lesser curvature of the stomach and no delay at the pylorus. It was interesting to find that the gall bladder filled rapidly and easily with the barium meal and presented a picture of a big duodenal pouch. There was no evidence of a chronic duodenal ulcer. The patient was kept in bed and treated medically and improved very considerably and in April, 1930, was free from symptoms, and his anæmia had recovered. In spite of the alkaline treatment, he had another attack of melena in January, 1931, and became very anæmic. He was seen by a physician and kept in bed on a

strict diet and made some improvement, but in August, 1931, it was again noted that he had blood in the stools. On September 15, he was readmitted to hospital complaining of a considerable amount of pain and tenderness; a blood examination showed only two and a half million red blood corpuscles. On September 18, 1931, a second operation was performed. Dense adhesions were found around the gall bladder and anastomosis and behind this could be felt a hard indurated area in the first part of the duodenum. The pancreas was smooth and very hard. It was thought that the duodenal ulcer was unquestionably due to removal of the alkaline juices, which were probably diminished by the presence of the pancreatitis, from the duodenum to the jejunum. The efferent loop from the cholecystenterostomy was therefore freed and brought up to the stomach, an anterior gastro-enterostomy being performed. The patient stood the operation very well and made an uninterrupted recovery. His pain disappeared, the blood count rapidly improved, and he ceased to pass blood in the stools. He has been seen from time to time in the follow-up department and the last note, September, 1932, states that he is very well, is on a full diet with no pain, the anæmia has completely disappeared and he is living a normal life.

In the first of these cases the pancreatic secretion was greatly diminished by the extensive pancreatectomy and thus failed to neutralize the gastric juice, although this was reduced by the partial gastrectomy. In the second case the pancreatic secretion was not only probably in part reduced by the pancreatitis but was made to enter the intestine at a considerable distance from the duodenum so that the gastric juice was not neutralized. Reduction of this juice in the one case and its adequate neutralization in the other brought about a complete cure.

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OSTEOCHONDRITIS OF THE GROWTH CENTERS

A Further Consideration[1]

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THE purposes of this paper are (1) to present three cases of osteochondritis of the growth centers, (2) to discuss and correlate the clinical and pathological aspects of the disease, (3) to present a method for the investigation of the pathogenesis of this condition, and (4) to urge the necessity of prolonged avoidance of weight-bearing in certain types of the disease.

Although the literature is rich in case reports and discussions of osteochondritis, there has been an almost complete absence of pathological studies. During the past year four unusual cases have been studied, and from three of these biopsies were obtained. These cases are presented with the thought that by a continuance of such studies the pathogenesis of osteochondritis may eventually become more clearly understood.

Harbin and Zollinger, in 1930, reviewed the pathological changes that occur in the various ossification centers of the human skeleton and called attention to the fact that a wide variety of terms are used to designate the same type of lesion occurring in different places. They proposed to simplify the confused nomenclature that has arisen because of the application of proper names to the disease in the various growth centers, by the use of the term "osteochondritis" in conjunction with the name of the growth center involved. The name of a disease should be descriptive of the pathological changes involved, and the term "epiphysitis" was deemed unsatisfactory because the disease is not confined to the epiphysis. It is recognized, too, that the term "osteochondritis" is not entirely descriptive, inasmuch as its inflammatory character is not fully established. The selection of a suitable name must await further pathological studies.

Zemansky, in 1928, gave a comprehensive summation of the literature regarding the pathological changes occurring in the capital epiphysis of the femur. Although all of the cases which he reported had some findings in common, they varied in detail. He concluded that the pathological changes occurring in this disease in the hip were: extensive subchondral necrosis of bone and marrow with complete destruction of the epiphyseal line; fragments of dead bone surrounded by richly vascularized granulation tissue; fibrous tissue replacement of necrotic areas with osteoid formation from fibrous tissue and pre-existing bone lamellæ; dilated blood vessels in the under surface of the cartilage. In the 11 cases which he summarized the epiphyseal line was present in cases of short duration, while in those cases extending over a longer period it was at least partially destroyed. Later Lippmann reported a case, focusing his observations principally on those occurring in the round ligament. In this he demonstrated obliterative thickening of the vessels with hæmorrhage and œdema of the ligament itself. In the case reported by Harbin and Zollinger there were no pathological changes seen in the specimen removed for biopsy. Vignard also reported 2 cases in which no change was observed. It is probable that in these latter cases the biopsy simply failed to include definite diseased areas.

Case 1. A white girl, aged 4 years, was originally admitted to the Rainbow Hospital with the complaint of stiffness in joints and weakness. She had been a full term, normal infant. Breast feedings were given for the first year, with the addition of cod liver oil and orange juice. The first teeth appeared at 7 months, and the remainder were normal in time of appearance. The child talked at 18 months and walked 1 month later. At that time it was noted by the mother that movement in all of the joints was limited, and that when the child walked the feet were turned outward at right angles to the body. In addition, the ankles, knees, wrists, and elbows were larger than normal, and she could walk only a short distance before becoming tired. The family physician said that she was underdeveloped, and he increased the amount of cod liver oil. She was seen later by another physician who made a diagnosis of severe rickets and she was treated following this with ultraviolet lamp

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Fig. 1.

Fig. 2.

Fig. 3.

Fig. 1. Enlargement of the malleoli, knees, and wrist in Case 1.

Fig. 2. There is marked irregularity and narrowing of the vertebral nuclei (Case 1).

Fig. 3. Changes seen in the lumbar spine are similar to those present in the dorsal segments (Case 1).

and given viosterol. She had always been subject to frequent colds and was underweight. It was noted by the parents that she frequently perspired about the forehead. The mother felt that she had shown little if any general improvement and that in addition she was becoming more round shouldered. There had been no gastro-intestinal upsets and the bowels were always regular.

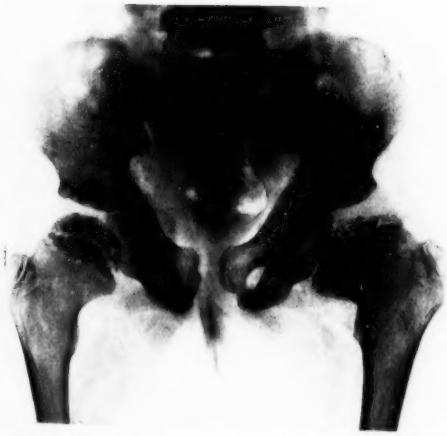

Fig. 4. Beside the changes characteristic of osteochondritis in the hip the pelvic girdle presents an abnormal degree of density (Case 1).

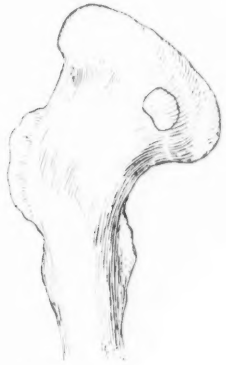

Fig. 5. Schematic illustration showing area from which tissue for biopsy was taken (Case 1).

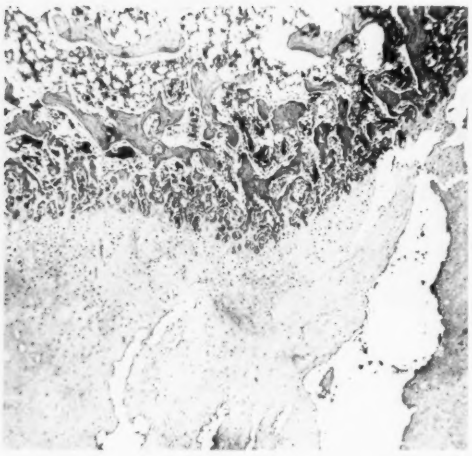

Fig. 6. Non-ossified epiphysis of femur comprised of hyaline cartilage which is the seat of fibrillar degeneration and extensive vascularization. ×70.

The 4 other children in the family were in excellent health. Parents were small in stature.

The physical examination revealed an underdeveloped and somewhat undernourished child with a generalized muscular weakness who was unable to stand without support or to walk for more than a short distance unaided (Fig. 1). The knees were flexed slightly when she walked. The head, eyes, ears, nose, and throat were normal. The teeth were normal and the tonsils were not enlarged. The heart and lungs were normal, and there was no gross evidence of rickets in the bony thorax. The spleen and liver were not palpable. The extremities showed weakness and atrophy that was most marked in the legs. The thenar and hypothenar eminences of both hands were flattened. The proximal interphalangeal joints of the third and fourth fingers of both hands were enlarged and fusiform in shape. The wrists were large and broad. There was no muscular atrophy of the arms or forearms, and movement in all the joints, except the right wrist, was within normal range. The right wrist showed marked spasm and limitation especially on hyperextension. The internal malleoli of both ankles were enlarged with thickening about the joints. The knees were enlarged with periarticular thickening but they were not tender. The left hip showed normal flexion with 5 degrees of adduction and 15 degrees of abduction. There was 5 degrees of internal rotation and 35 degrees of external rotation. The right hip showed unlimited flexion with 45 degrees of motion in both abduction and adduction. Internal rotation was limited to 10 degrees with 45 degrees external. Motion was painless. The usual reflexes were present and equally active. The spine showed a moderate dorsal kyphosis with rounded shoulders.

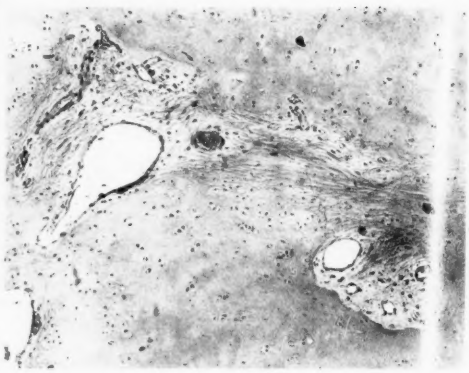

Fig. 7. Articular cartilage showing active vascularization with formation of trabeculæ of osteoid. Zone of proliferate cartilage is not unusual and the zone of provisional calcification is not apparent. Extensive degeneration, laceration, and vascularization of cartilage. ×20.

Roentgenograms showed the dorsal and lumbar vertebræ to be irregular in outline, mainly in their anterior portions (Figs. 2 and 3). The intervertebral spaces were maintained throughout but the bodies were flattened. The capital epiphyses of both femora were flattened and irregular (Fig. 4). This was most marked on the left where there was fragmentation and some evidence of migration of the head toward the trochanter. The necks were very short and greatly thickened but the epiphyseal lines could be seen. A similar process was seen in the heads of both humeri, the condyles of the femora, and the patellæ. These changes were also seen but to a less extent in the ankles, wrists, and the metacarpals.

Laboratory examination showed no abnormalities of the urine or blood. The blood Wassermann was negative. The basal metabolic rate was increased 21 per cent. The blood serum calcium was 10.6 milligrams per 100 cubic centimeters and the phosphorus was 4.5 milligrams.

The patient was placed in the dorsal decubitus position on a hyperextended Bradford frame because of the dorsal kyphosis. Free use of the extremities was encouraged by physiotherapy, including exercises in the underwater gymnasium. A fairly constant range of temperature from 37.5° C. to 38° C. (rectal) was observed. She showed slight general improvement, and, on December 9, 1931, an exploration of the left hip was carried out through an anterior incision.

At operation the capsule was found to be normal. The head was definitely enlarged and the neck was short and thick, but there were no other gross abnormalities. The acetabulum was normal in appearance. Tissue for biopsy was removed from the region of the epiphyseal line including the adjacent tissue (Fig. 5). The tissue was softened but well vascularized.

Fig. 8. Early change in the right hip. There is only slight flattening of the head and shortening of the neck (Case 2).

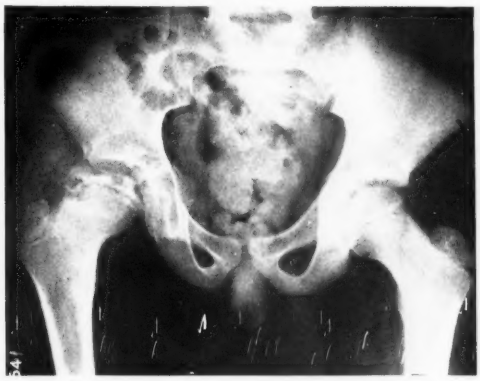

Fig. 9. Presents a marked degree of progression of the disease in the capital epiphysis on the right with fragmentation of the head (Case 2).

Motion was restricted only by a crinolin spica and convalescence was uneventful without febrile reaction. Aerobic and anaerobic cultures were negative.

The specimen submitted for pathological examination consisted of a cylinder taken from the head of the femur so as to include the entire thickness of the articular cartilage, the bony epiphysis, and the epiphyseal plate of cartilage. The bony changes were not remarkable and appeared to be secondary rather than primary. In spite of the marked deformity of the head of the bone seen roentgenologically, the general pattern and structure of the trabeculæ were normal. The density varied with osteoporosis predominating. The marrow was not unusual except in the subchondral zone where it was fibrous. There was no necrosis and no hæmorrhage. The articular and epiphyseal chondro-osseous junctions were very irregular. The primary spongiosa in both situations was poorly calcified and preponderantly of osteoid. The zone of provisional calcification was irregular and poorly defined. Enchondral vascularization was very pronounced and the penetrating blood vessels were found at greater distances from the marrow than usual. These vessels were surrounded by collars of osteoid and frequently by wide zones of proliferating fibroblasts. Despite the vascularization, the enchondral ossification was focal and generally retarded. This retardation seemed best accounted for by the severe degenerative changes present in the cartilage. Foci of degeneration and necrosis were scattered throughout the epiphyseal and articular cartilage, and in the latter there were deep fissures and tears, sometimes reaching the chondro-osseous junction. (Fig. 6). Areas of resting cartilage were interposed between areas of cartilaginous hyperplasia, and the hyperplastic foci were almost invariably associated

Fig. 10. Diagram indicating the point of removal of tissue for biopsy (Case 2).

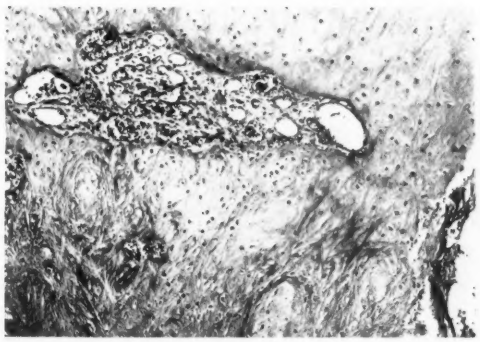

Fig. 11. Articular cartilage, Case 2, including a group of ingrowing marrow vessels at the edge of an area of cartilaginous degeneration. There has been focal absorption of the matrix which has taken on a fibrillar character. Such areas are especially well vascularized but without ossification. ×65.

Fig. 12. Presents very slight change in the right hip. The head is slightly flattened. (Case 3.)

Fig. 13. Shows rapid progression of the disease with irregularity and fragmentation of the head but no appreciable thickening of the neck. The epiphyseal line is irregular. (Case 3.)

with disintegration of the matrix. Much of the vascularization with accompanying fibroblastic proliferation appeared to be in the nature of a repair process, where there had been dissolution of the original hyaline cartilage (Fig. 7).

Since the foregoing procedure was carried out, the patient has been given general hygienic treatment, including ultraviolet lamp therapy and cod liver oil. Her posture has improved slightly, but her general condition shows but little change.

CASE 2. A white boy of 8 years was admitted to Lakeside Hospital in January, 1931, with the complaint of pain in the right hip and a limp of 2 months' duration. There was an indefinite history of a fall at the beginning of the illness. Examination at that time showed a few carious teeth and enlarged tonsils. The extremities were normal except for the right hip. There was flattening of the buttock and 1 inch atrophy of the thigh. Palpation revealed no peri-articular thickening or tenderness. Motion was limited in abduction and internal rotation. Roentgenograms of the hip showed some flattening of the capital epiphysis with definite increased density in a portion of it (Fig. 8). Urine and blood studies were normal. The blood Wassermann reaction was negative, and the tuberculin test, 1-1000, was negative. The patient remained in bed but showed no clinical improvement in the hip, and a plaster spica was applied on February 18, 1931. This was removed after 6 months, but after he was allowed up a limp was immediately noted. He denied any pain, and the roentgenogram showed only a slight increase in density of the epiphysis.

In February, 1932, he was readmitted to the hospital with the complaint of a dull aching pain in the right hip which always appeared after walking or playing for a short time. Examination revealed the right leg to be 0.5 inch shorter than the left. The right buttock was flat, and there was 2 inches atrophy of the thigh. Motion at the hip showed abduction of 25 degrees, flexion of 15 degrees, internal rotation of 5 degrees, and external rotation of 10 degrees. There was no palpable tenderness or thickening. Roentgenograms showed progressive flattening and fragmentation of the capital epiphysis on the right (Fig. 9). The blood Wassermann reaction was negative, and the tuberculin test, 1-1000, was negative. The serum calcium was 11.2 milligrams per 100 cubic centimeters of blood and the serum phosphorus was 4.9.

On February 16, 1932, an exploration of the right hip was carried out through an anterior incision. The synovia was thickened and hyperæmic. There was increased fluid in the joint. The head of the femur was large and smooth and capped over a shortened neck. Across the top of the head was a groove that corresponded to the position of the upper margin of the acetabulum as it rested against the large head. The acetabulum was of normal size and depth but too small for the head. There was no evidence of a round ligament. The epiphyseal line was identified and two blocks of tissue were removed from the epiphysis with an osteotome (Fig. 10). Aerobic and anaerobic cultures were taken from the joint and the depths of the wound from which the tissue was removed.

The gross specimen showed what appeared to be islands of cartilage in bone tissue. Microscopically there was marginal thickening of the articular cartilage. Scattered through the cartilage were

degenerative foci ranging from fibrillation to necrosis. In the fibrillary areas around the small blood vessels the matrix was absorbed and the vessels were surrounded by actively proliferating fibroblasts to produce small cellular islands (Fig. 11). The chondro-osseous junction was quite irregular and the bony lamella thin and interrupted. The most conspicuous change seen was simple rarefaction of the matrix, and in some instances this was associated with the granular deposition of calcium. Independent islands of bone with fatty marrow were seen in the cartilage. The synovia was thrown into polypoid folds and the lining cells were hyperplastic. Beneath the surface the synovia was richly vascularized and there was considerable lymphocytic infiltration that was characteristically perivascular. Staphylococcus albus grew in aerobic and anaerobic cultures.

Convalescence was uneventful and the patient's condition has remained about the same. Roentgenograms show a slight increase in the amount of fragmentation. He has been given cod liver oil and ultraviolet lamp therapy as a general measure and has not been allowed to bear weight on the involved extremity.

CASE 3. A white boy, aged 4 years, was first admitted to Rainbow Hospital August, 1931, because of a painful right hip. The onset of the complaint had occurred very suddenly in June, 1931, when he first complained of pain. Soon after this a limp was noted by the members of his family. This lasted for about 1 week and then disappeared; however, it recurred about 10 days later and was so severe that he could not walk. Roentgenograms showed very slight flattening of the capital epiphysis on the right (Fig. 12). He was placed on a Bradford frame with the leg in traction. By November 28, 1931, all physical signs had disappeared, and he was allowed to go home. He returned 1 month later with reappearance of all symptoms with increased severity and in addition a history of *night cries*. His past history revealed only an attack of mumps, frequent colds, and sore throats.

The physical examination showed a moderately well developed but somewhat undernourished white boy. The examination was essentially normal except for the right lower extremity. There was no shortening of the right leg but there was 1 inch atrophy of the thigh. Palpation revealed no tenderness, but there was marked spasm with any attempt at motion. Internal rotation and hyperextension were completely limited and abduction was limited to 10 degrees. Roentgenograms showed definite flattening of the capital epiphysis with some fragmentation (Fig. 13). The neck was hazy and irregular with two small punched out areas in the diaphyseal side of the epiphyseal line. The urine was normal. The Wassermann test was negative; tuberculin test, 1-1000, was negative. The serum calcium was 10.4 milligrams per 100 cubic centimeters of blood and the serum phosphorus was 4.7 milligrams.

Fig. 14. Diagram showing the points of removal of the tissue for biopsy. (Case 3.)

Following admission he was placed in traction, and the pain and spasm grew less. On January 30, 1932, because of the unusual appearance the hip was explored through an anterior incision. It was our impression before operation that we were dealing with an osteitis rather than an osteochondritis. The capsule was found to be thickened and hyperæmic with some increase in fluid. The head and neck showed no gross abnormalities and the acetabulum appeared normal. A block of tissue was removed from the epiphyseal line with an osteotome (Fig. 14). The tissue did not appear to be as well vascularized as normally and the material was softer than usual. Microscopic study showed foci of degeneration in the cartilage which were in places myxomatous and in others fibrillar. Such degenerate foci were sharply circumscribed (Fig. 15), and occasionally associated with vascularization and beginning calcification. There was a moderately severe osteoporosis. Cultures showed no growth.

Convalescence was uneventful and the patient was again placed in traction. Gradually all spasm and limitations have disappeared and at present there is no limitation of motion. He has not been allowed to bear weight on the extremity for almost 5 months, however. Recent roentgenograms show some slight fragmentation of the epiphysis.

The fourth case is presented to show the striking similarity of arthropathy of the tarsal scaphoid to osteochondritis.

CASE 4. A white boy, aged 12 years, was admitted to the hospital with the complaint of swelling of the feet. At the age of 3 the patient had an attack of diphtheria and some time following this the mother noticed that his legs were weak and that it was more difficult for him to walk than it had been previously. This condition remained about the same until he

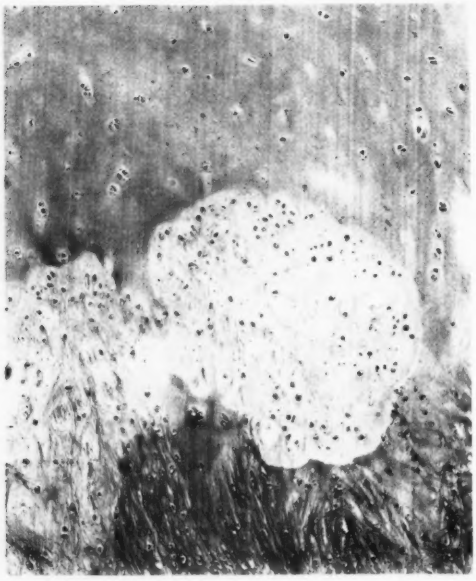

Fig. 15. Epiphyseal plate showing normal hyaline cartilage at the top separated from the degenerate cartilage at the bottom by an area of cartilaginous regeneration and proliferation. Such spontaneous repair was not a prominent feature, the degenerate areas usually being vascularized and collapsed. ×81.

was 10 when it was noted that he was walking on his toes with the feet turned in. In August, 1931, the patient noticed, while running barefoot, that the right foot was swollen and a little tender. The swelling persisted up until the time of admission to the hospital, without pain. There was no history of injury, chills or fever, or of poliomyelitis. His general health had always been good.

The mother and father were cousins. There were four children in the family. The oldest had had no difficulty. The next oldest boy had been in the hospital repeatedly with a complaint somewhat similar to that of this patient; in addition he has shown marked loss of sensation with trophic disturbances in the lower extremities. The youngest child, a girl, is normal except for a cardiac lesion, thought to be rheumatic in origin.

The physical examination showed a fairly well developed, somewhat undernourished, white boy whose examination was not remarkable except for the lower extremities. The legs showed atrophy with complete relaxation of the longitudinal arches in both feet. The tendo achillis on each side was tight and prevented dorsiflexion of the foot even up to a right angle. The legs were equal in length and the muscle power below the knees was very poor except for the gastrocnemii. He was unable to invert the foot at all and the peroneals were only

Fig. 16. The right foot in the lateral position shows compression and fragmentation of the scaphoid. A lateral film of the left foot illustrates the same character of change in the head of the astragalus. (Case 4.)

moderately strong. There was swelling with periarticular thickening over the dorsum of both feet, most marked over the right in the region of the scaphoid where there was local heat and redness, but there was no pain or tenderness in either foot. When he walked he rose on his toes with the knees flexed. The toes and knees were pointed inward to maintain balance. He walked with a peculiar shuffling, scissors-like gait as he lurched from side to side and swung the arms to keep from falling. The reflexes in the arms, abdominals, epigastrics, and cremasterics were normal. In the lower extremities the reflexes were hyperactive with both patellar and ankle clonus. The latter was a constantly sustained response, the former only occasionally. There was a Babinski response to plantar stimulation on both sides and the Romberg test was positive. The cranial nerves showed no involvement and the eyegrounds were normal. There was weakness of the lower abdominal muscles. There was no change in sensation over any portion of the body and the joint sense was normal. There was no ataxia, no intention tremor, no past pointing. Speech was difficult. The vibratory sense was not lost.

Roentgenograms of the feet (Fig. 16) showed a destructive process involving the right scaphoid and the anterior portion of the astragalus. On the left the astragalus alone was involved. The bony arches were flattened. The spine showed no abnormality.

Laboratory studies showed the urine and blood to be normal. The Wassermann reaction was negative. The tuberculin test, 1-1000, was negative. The serum phosphorus was 4.3 milligrams per 100 cubic centimeters of blood and the serum calcium was 10.3 milligrams. The spinal fluid was clear and colorless. The Pandy test was negative and there were no cells. The Wassermann test was also negative.

The patient was kept in bed over a period of weeks until the redness and swelling had disappeared.

Since he has been allowed to walk his condition has changed very little except that under training his gait has somewhat improved. We believe this to be a case of *hereditary family spastic paraplegia* with changes in the bones of the feet resembling osteochondritis but probably an arthropathy.

The first patient presented several rather perplexing problems. She was the first patient that we have seen or of whom we have heard in whom the condition was generalized. When first seen she had the appearance of having polyarthritis with enlargement and stiffness of all the joints. The involvement of all the epiphyses and particularly the appearance of the hands suggested achondroplasia but there was no disparity in comparison between the length of the torso and the extremities. The normal blood serum calcium and phosphorus, absence of certain stigmata, and the roentgenographical appearance helped to rule out rickets.

Harbin and Zollinger reported one family in which four individuals showed osteochondritis of the spine. Such observations together with this case cause one to consider again both hereditary and metabolic factors in the etiology in these individual cases.

The second patient was given the benefit of immobilization over a period as long as that in which many cases have begun to show clinical improvement. It is evident that the process was not healing, since with weight-bearing the condition progressed and the signs returned once more. The roentgenographical picture was then striking as compared with the earlier one showing only slight flattening and areas of increased density. At operation there was found evidence of inflammatory change in synovia, joint, and bone. Four cultures were taken in all, two aerobic and two anaerobic, and all showed staphylococcus albus. This is the first positive culture that we have ever obtained from a patient with osteochondritis; it suggests again a consideration of infection as an etiological factor, but only in this individual case. The condition, therefore, may be one of osteitis rather than osteochondritis.

The third patient was immediately immobilized with the acute onset. At that time we felt that such a long period of immobilization was not necessary and he was allowed to run about after the acute signs had disappeared. Within a short time the acute symptoms returned and it is evident from the roentgenograms that the disease had progressed rapidly. It is of interest that the clinical signs and symptoms have again disappeared, but he has not been allowed to bear weight at this time.

It would appear that the pathological picture in these cases varies from that described by previous observers in that instead of describing and discussing a different condition we are seeing merely different phases in the pathogenesis of the same condition. Beyond doubt, all of the cases described, except possibly Case 2, can be clearly classified as osteochondritis of the capital epiphysis from the appearance of the roentgenograms. We did not remove the entire head in any case as we felt that in such young individuals such treatment is too radical. It is true that in older individuals we see frequently an arthritis of the hip which we ascribe to an old osteochondritis. In such cases, excellent results have followed the Whitman reconstruction operation. In growing children, however, we believe that removal of the head will aid in preventing later arthritis. It will also prevent further growth from this important center, and for that reason is not a procedure of choice.

The pathological changes observed in all 3 cases were similar in that the cartilage, both articular and epiphyseal, was the seat of the most striking alteration. The osteoporosis of the epiphysis could be explained by the inactivity, rather than as a feature of the disease. The irregularity in density of the osseous head was thought to be due to the irregular retardation of enchondral ossification and to the production of osteoid rather than bone. The asymmetry and non-development (apparent destruction) of the head seemed better accounted for as a failure in new bone formation, rather than as a destruction of already formed bone, inasmuch as the former was seen to be true, while there was no necrosis or unusual osteoclasis to indicate the latter. This lack of ossification was related to, if not caused by, a deterioration of cartilage, which was focal and which ranged

from simple fibrillation to necrosis of cells and dissolution of matrix. The cartilage was so severely altered that despite the relative inactivity of these individuals deep fissures and tears through the entire articular plate were observed. The cause of the cartilaginous degeneration was not apparent, although faulty nutrition is obviously suggested. Harbin and Moritz called attention to the presence of interlacunar canaliculi in the matrix of hyaline cartilage, and suggested the importance of these canaliculi in the dissemination of nutritive substances throughout cartilage. The primary defect responsible for the imperfect ossification of the epiphysis may rest in the lack of permeability of the cartilaginous matrix, with subsequent degeneration so as to inhibit proper enchondral ossification. The fact that the cartilage was so richly vascularized does not militate against this hypothesis, because the presence of the blood vessels may represent an attempted compensation, or may be regarded as a reparative process for the necrosis.

Microscopic evidence of inflammation was not seen either in bone or cartilage. The chronic hyperplastic synovitis observed in one case was not explained.

We must conclude that the necrosis and repair of bone described by Zemansky was either a different phase of the disease than seen by us or a manifestation of greater severity. The latter belief seems more tenable, if one accepts the hypothesis of the repaired nutrition to explain the cause of the epiphyseal change. Whereas in the cases seen by us the cartilage was damaged to the extent of being unsuitable for enchondral ossification, it is not difficult to consider the same process becoming extended to include the bone and cause the necrosis described by other authors.

In order to complete the pathological picture the entire pathogenesis must be seen and studied. This can be accomplished if complete clinical and laboratory study of all cases is made followed by a biopsy according to the "Key block method." It will then be possible to correlate pathological change with the gross and roentgenographical appearance. Large numbers of such cases will eventually result in a varied picture which if viewed with sufficient perspective may allow us to gain a clear conception of the etiology of osteochondritis. We have reason to think that years are necessary for healing to take place in this disease, and that alone would seem to account for a great part in the variation of the histopathology.

SUMMARY

1. Three cases of osteochondritis are reported with clinical findings and associated pathological change. One of these cases showed a generalized involvement of growth centers, the first of its kind ever to have been published.

2. An attempt is made to correlate the varied pathological reports from the literature.

3. A method is offered as an aid in obtaining the complete pathology, and the etiology is discussed.

The authors wish to thank Dr. Alan R. Moritz for the preparation of the photomicrographs.

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THE RELATION OF MATERNAL METABOLISM TO INFANT BIRTH WEIGHT

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THE factors which influence intra-uterine development of the fetus and its weight at birth remain obscure although the problem has been attacked both in man and in experimental animals from many angles.

The assumption of a relationship between maternal weight and maternal diet during pregnancy to infant birth weight seems so probable that it has been studied exhaustively (1, 4, 5, 6, 7, 8, 13, 17, 22). The results, however, have been for the most part negative, and it is now generally believed that diet plays no rôle of consequence in influencing the birth weight of the newborn. There is experimental evidence to show that healthy, well-nourished rats produce litters of greater total weight than smaller animals fed on a deficient diet (7, 8), but the variation is so small as to be quite negligible. The opinion of present day investigators may best be summed up in the statement of Franz and Zondek, quoted by Jonen (4): "The fetus develops without consideration of the maternal organism and like a parasite withdraws what it finds necessary to its composition." If the maternal organism does not provide the materials necessary for fetal development, damage to, or death of, the fetus results, with subsequent abortion (4, 5, 8, 17, 22); but without noticeable effect on birth weight.

Other maternal factors which have received attention include age (1, 7), social status (15), national disturbances such as war (14), number of previous pregnancies (7, 15, 24), whether or not previous offspring have been suckled (1), length of pregnancy (2, 7, 18), seasonal variations (1, 16, 24), primiparity versus multiparity (9, 15), and the duration of the menses (9, 21). With the exception of the last named, such factors bear only an insignificant relationship to birth weight, influencing average infant weights less than 100 grams. The older the mother the greater the birth weight, and the more unfavorable the social status and the greater the national disturbance the more unfavorably fetal development is affected. If previous offspring were suckled, birth weights decrease in subsequent pregnancies. In general, infant birth weight is greater in summer than in winter. The birth weight tends to increase with the number of pregnancies.

Matarese, and Szenes and Mondré, listing 400 and 739 human births, respectively, point out the correlation between length of menstrual period and infant birth weight and show that weight and length of the child at birth are directly proportional to the duration of the menses in days.

The nutrition of the father has been studied in animals (8) but no relationship was observed.

The action of the various vitamins has been investigated in attempts to clarify the problem (8, 12, 16, 17, 22, 23), but the results have been no more convincing than other starvation experiments along the same lines. Depletion of vitamins produces fetal damage (8, 17, 22) and abortion, while an increase in vitamin D in the maternal diet influences intra-uterine development favorably (12, 22) and is an aid in hindering habitual antepartum fetal death (12).

The placenta has been studied from the standpoint of iron content (3) and of architectonic structure of the blood vessels (20). The iron content of 100 grams of placenta was correlated with birth weight and was found to vary directly with the birth weight in children below normal limits, reaching its highest value in children in the usual range (2,800 to 3,500 grams) and then decreasing in the higher weight groupings. Shordania found that there was a tendency to lower placental and fetal weights if there was great diffusion of the main vessels of the placenta.

PURPOSE OF PRESENT STUDY

The present study was suggested by certain unpublished data indicating sectional differences in average birth weights, and was

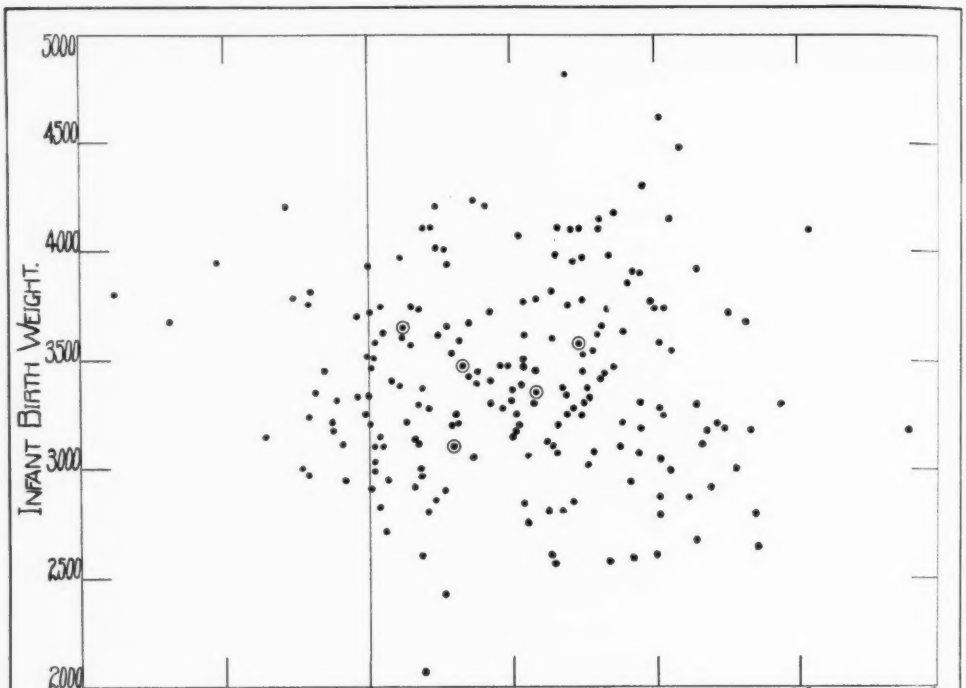

Fig. 1. Scatter diagram of distribution of basal metabolic rates of 203 pregnant women and weights of their infants at birth. Horizontal axis: maternal basal metabolic rates. Vertical axis: Infant birth weights in grams. Nine infants weighing less than 2,000 grams are not included. Dots enclosed by circles represent two determinations falling at the same point on the chart. Note that there is no visible relationship between the two variables.

planned to determine whether a relationship exists between maternal basal metabolic rate and infant birth weight. With Matarese and Szenes and Mondré claiming that prolonged menstrual periods correlate with greater infant birth weights and with menorrhagia known to be associated with moderate hyperthyroidism, it is suggested that low basal metabolic rates should correlate with large, and high rates with small babies.

METHOD

Basal metabolic rates, each reading comprising a trial and an actual test, were done on 212 normal, pregnant women taken in order of admission to the Obstetrical Service of the University Hospital. A few of these women were occasionally admitted some weeks before delivery, so that in an exceptional instance a reading was obtained as early as 80 days prior to the onset of labor, although the majority were made within 30 days of labor. The determinations were made as soon after admission as the women were adjusted to routine hospital life, and were done by the indirect method based upon oxygen consumption with the respiratory quotient assumed to be 0.82, and the Roth-Benedict apparatus being used. They were done according to the routine hospital technique and were interspersed with the daily work of the metabolic laboratory insuring reasonably consistent data, although the emotional element was not necessarily completely controlled. Only a

TABLE I.—MATERNAL BASAL METABOLIC RATES, AVERAGED ACCORDING TO INFANT WEIGHT GROUPINGS

Birth weight of infants—grams	Average maternal B.M.R. (added algebraically)	Number of cases	Range of maternal B.M.R.
2,000 to 2,499	+11.0	3	+ 4.0 to +33.0
2,500 to 2,999	+11.9	30	− 4.2 to +27.1
3,000 to 3,499	+10.0	92	− 7.2 to +37.8
3,500 to 3,999	+ 9.0	57	−17.7 to +25.9
4,000 to 4,499	+11.2	19	− 5.7 to +30.6
4,500 to 4,999	+17.1	2	+13.9 to +20.3

Nine infants weighed less than 2,000 grams and were not included in this table. Note that no relationship between the two variables, infant birth weight and maternal basal metabolic rate, is demonstrated.

single reading was obtained on each patient although the advisability of repeated tests is well recognized.

RESULTS

The maternal basal rates as determined, ranged from minus 17.7 to plus 37.8, while the birth weights of the babies varied from 780 to 4,814 grams. Evaluation of the collected data was carried out in three ways.

The infant birth weights were arranged arbitrarily into six groups ranging from 2,000 to 4,999 grams in steps of 500 grams, and the average maternal basal metabolic rate calculated for each group (Table I). Also the metabolic rates were arranged in six groupings, and the average infant birth weight computed for each group (Table II). Nine infants weighed less than 2,000 grams and were not included in either table. Neither arrangement of the data shows any significant differences among the computed group averages.

A scatter diagram (Fig. 1) was drawn, with maternal basal metabolic rates plotted along the horizontal axis and infant birth weights along the vertical axis. The lack of a relationship between basal metabolic rate and infant birth weight may readily be seen by a glance at the graph.

Finally, correlations were computed for the series of 212 patients and a resulting coefficient of minus 0.087± a probable error of 0.046 obtained. Such a low correlation indicates definitely that so far as the data of the present

TABLE II.—INFANT BIRTH WEIGHTS, AVERAGED ACCORDING TO METABOLIC RATE GROUPINGS

Maternal B.M.R.	Average I.B.W., grams	Cases	Range of infant birth weights, grams
−20.0 to −10.1	3,801.0	4	3,688 to 3,950
−10.0 to − 0.1	3,376.6	18	2,946 to 4,200
0.0 to +10.0	3,383.1	73	2,060 to 4,230
+10.1 to +20.0	3,456.3	79	2,574 to 4,814
+20.1 to +30.0	3,258.1	26	2,655 to 4,615
+30.1 to +40.0	3,651.1	3	3,178 to 4,098

Nine infants weighed less than 2,000 grams and were not included in this table. Note that no relationship between the two variables, maternal basal metabolic rate and infant birth weight, is demonstrated.

study go, no relationship exists between maternal basal metabolic rate and infant birth weight.

CONCLUSIONS

No predominating factor influencing infant birth weight has yet been demonstrated.

No relation was demonstrated between single basal metabolic rate determinations, done by the indirect method, on 212 normal, healthy pregnant women and the birth weights of their children.

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THE EFFECT OF PERITONEAL IRRITATION ON THE EMPTYING TIME OF THE GALL BLADDER AND STOMACH

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THE rôle of the sympathetic nervous system in relation to the altered function of various portions of the gastrointestinal tract has in recent years attracted much attention. The work reported in this paper was undertaken for the purpose of establishing a functional relationship between the autonomic nervous system and the gall bladder, if such existed, and to determine whether this effect was one of excitation or inhibition. The response of the gall bladder to remote peritoneal irritation offered a means of obtaining further evidence regarding the functioning of the gall bladder and also the possible relationship of the sympathetic nervous system to this organ. The effect of such peritoneal stimulation on the gall bladder was studied by means of roentgenograms following the intravenous injection of sodium tetraiodophthalein. The filling and emptying time as well as the ability of the gall bladder to concentrate the dye were observed and this correlated with the emptying time of the stomach as determined by roentgenograms following a barium meal.

That the gall bladder has a relatively rich nerve supply of both medullated and nonmedullated fibers has been well established, but the connections of these fibers, and particularly their relations to the vagus and splanchnic nerves, have not been clearly defined from an anatomical viewpoint. The functions of this abundant nerve supply have been the object of much investigation, but, unfortunately, due partly to the variety of experimental procedures used, there have been many conflicting results. The earlier studies were chiefly directed toward the vagus and splanchnic nerves in an effort to establish their specified functions as regards the gall bladder, and the earlier investigators such as Heidenhain and Doyon believed that the splanchnic nerves were motor to the gall bladder. At a later date Courtade and Guyon, Bainbridge and Dale, Lieb and McWhorter, Westphal, and others concluded that the vagus was the motor nerve to the gall bladder. Bainbridge and Dale also showed that splanchnic stimulation resulted in relaxation of the gall bladder. Freese concluded that the splanchnics contained both motor and inhibitory fibers. Mann, in summing up the literature in 1924, concluded that "as is seemingly true with the other viscera all the motor and inhibitory fibers do not run in the same nerves, but some of each are found in the vagus and splanchnic; nevertheless the vagus is mainly motor and the splanchnic mainly inhibitory to the gall bladder." All of the data were based on direct observation of the exposed or isolated gall bladder or on changes in pressure within the biliary system. In most instances, the nerves were stimulated electrically and in some the changes were based on the action of drugs.

The advent of a means of visualizing the intact gall bladder permitted an experimental approach much more closely simulating normal physiology. Whitaker was the first to use this means of studying the nervous control of the gall bladder. His method was to inject iodized oil into the gall bladder, following which he stimulated the nerves both centrally and peripherally. His conclusions were that the vagus and splanchnic nerves played no essential rôle in the emptying of the gall bladder. Boyden (3) observed that adrenalin was very effective in producing a diminution in the size of the gall-bladder shadow, and interpreted this as a contraction of the gall-bladder musculature, although Burget thought this escape of bile could be accounted for by relaxation of the duodenum induced by the adrenalin. Copher, Kodoma and Graham (7, 8) studied the effects of electrical stimulation of the vagus in dogs following the intravenous injection of suitable dyes for visualizing the gall bladder. Their results suggested some

control of the vagi over the gall bladder, but were not conclusive. They were unable to arrive at definite conclusions regarding the control of the sympathetic nervous system over the gall bladder.

Hughson (14) in 1925 reported a series of experiments on dogs in which he studied the emptying time of the stomach before and after peritoneal irritation, such as cauterization of the appendix. He concluded that, "Traumatization of any abdominal viscus in dogs by surgical procedure increases this emptying time approximately 67 per cent for a period of about two weeks." This type of experimental procedure more closely simulates the normal physiological response than does the electrical stimulation of the nerves. Furthermore it would seem to indicate that an animal on which an operation has been performed can no longer be considered as having a normal physiological response of the viscera until a considerable period has elapsed which varies with the individual animal. In 1927 Hughson (15) reported the effects of section of the vagus trunks and found that it was impossible to produce a reflex pylorospasm (after section of the vagus) by peritoneal irritation. He concluded that this established the efferent rôle of the vagus in the visceral reflex involving contraction of the pylorus as a result of peritoneal irritation.

Since the experimental results of vagus and splanchnic stimulation have yielded such conflicting evidence and since it is well known that the acute experiment on animals cannot always be used to interpret findings in the human organism as a result of disease, it was thought that the method of remote peritoneal irritation might be used to demonstrate the relationship between the gall bladder and the automonic nervous system.

METHOD

Dogs were used in these experiments and were selected according to their adaptability to training. They were given a diet of dog biscuit, casein mixture plus vitavose and milk, except when they received a test meal as devised by Boyden consisting of the yolks of six eggs and one half pint of cream. Inasmuch as it was necessary to avoid the use of anæsthetics the dogs were previously trained to lie quietly without restraint while the roentgenograms were taken. The dye used was sodium tetraiodophthalein, manufactured by the National Aniline and Chemical Company. After trial the optimum dose was found to be .17 grams per kilogram of body weight. This amount enabled one to obtain a clear visualization of the gall bladder without causing toxic reactions such as nausea, vomiting, and diarrhœa. Inasmuch as there was considerable variation in the individual response it seemed undesirable to use averages, and hence the following typical protocols are selected from the twenty animals used.

ILLUSTRATIVE PROTOCOLS

Dog 9. Adult female terrier, weighing 9.6 kilograms. This dog was given an intravenous injection of 1.63 grams of sodium tetraiodophthalein with no untoward reaction. The maximum gall-bladder shadow was obtained at the end of the fourth hour, and was emptied by the end of the fourth hour following the routine fat meal. The intravenous injection of the dye was repeated 2 weeks later and the same result was obtained. The emptying time of the stomach was determined by giving the animal a meal of barium sulphate, casein, crackers, and water as previously described. The stomach was completely empty at the end of 5 hours. This emptying time was again checked 1 week later with the same result. The dog was then operated on under ether anæsthesia. A low midline incision was used and the terminal ileum was vigorously rubbed with gauze. The dog made an uneventful recovery. One week following this operative procedure, the stomach did not empty until the end of the eighth hour (3 hours delay), and the gall bladder was not emptied until the end of the sixth hour (2 hours delay). The maximum concentration of the dye was the same as before operation. Sixteen days after operation the stomach and gall bladder again emptied within normal limits.

Dog 10. Adult male terrier, weighing 12.1 kilograms. The emptying time of the gall bladder and the stomach were determined in the same manner as in Dog 9. The emptying time of the gall bladder was found to be 9 hours and that of the stomach 8 hours. Both of these results checked within 1 hour on subsequent determinations. The dog was then operated on under ether anæsthesia. The appendix was removed, and the terminal ileum was rubbed with gauze. The animal made an uneventful recovery and the emptying time of the stomach and gall bladder were again determined. On the fourth day after operation the dog was given the same amount of sodium tetraiodophthalein as before operation. Roentgenographic examinations were continued at

intervals up to 22 hours, at which time the gall-bladder shadow was still clearly visible and had diminished very little in size. On the fifth day after operation the emptying time of the stomach was determined, and it was found not to empty until the nineteenth hour. Twelve days after operation the same tests were repeated and the stomach and gall bladder were again found to function within normal limits.

Dog 11. Young female terrier weighing 10.2 kilograms. This dog received the usual amount of sodium tetraiodophthalein (.17 grams per kilogram) and after the fat meal the gall bladder was found to empty in 6 hours. Following the usual barium meal the stomach was found to empty in 5 hours. Both of these results were found to check on subsequent trials. The dog was then operated on under ether anæsthesia. This incision was then closed with a Connell stitch. The abdomen was closed in the usual manner. Following an uneventful recovery, the emptying time of the gall bladder and stomach were determined 1 week after operation, at which time the gall bladder was found to empty in 9 hours (3 hours delay), and the stomach emptied at the end of the eighth hour (3 hours delay). At the end of the second postoperative week the stomach and gall bladder were again found to empty within normal limits.

Dog 12. Young male collie, weighing 8.6 kilograms. This dog received the usual intravenous injection (.17 grams per kilogram) of sodium tetraiodophthalein with no untoward reaction. The maximum gall-bladder shadow appeared at the end of the fifth hour and was completely empty 5 hours after the routine fat meal. The stomach was found to empty 7 hours after the test meal. Both of these results were checked on subsequent examinations. The dog was operated on under ether anæsthesia and a linear incision was made in the appendix with the cautery. This incision was then closed by means of a Connell stitch. The abdomen was closed in the usual manner. Nine days after operation the stomach emptied in 9 hours, showing a delay of 2 hours. On the tenth postoperative day the maximum shadow of the gall bladder was obtained 5 hours after injection of the dye and did not disappear until after 9 hours following the fat meal (4 hours delay). By the third week the gall bladder and stomach were again functioning normally as shown by the roentgenograms.

The experimental studies by Hughson (14) showing the delay in the emptying time of the stomach as a result of peritoneal irritation suggested that direct observation of the motility of an organ within the peritoneal cavity may not be a true representation of the normal functioning of this organ. These observations have been confirmed by the present work and in these experiments it has been found that the emptying time of the stomach is delayed even more (75 per cent) than that reported by Hughson (65 per cent). In addition the emptying time of the gall bladder was found to be delayed on an average of 80 per cent. In most of the experiments, the stomach and gall bladder were found to have a normal motility at the end of 2 weeks. The normal emptying time of both the stomach and the gall bladder was found to have considerable variation in different dogs; the minimum emptying time of the gall bladder in the normal dog was 4 hours, and the maximum 9 hours. The minimum emptying time of the stomach was found to be 5 hours and the maximum 8 hours. However, the normal emptying time repeated in the same animal checked very closely. Because of these variations in the normal animal, averages do not represent an accurate picture of the result of the experimental procedure. The concentration of the dye in the gall bladder as far as could be determined by roentgenographic study remained essentially the same, whether or not the emptying time of the gall bladder was delayed.

Observations on the mechanism by which this delay is brought about have not been completed and will be reported elsewhere. However, in view of the fact that the delay in the emptying time of the gall bladder roughly parallels the delay in the emptying time of the stomach, it might be assumed that there is a casual relationship, possibly, as has been suggested, the result of food passing into the duodenum. However, even though the emptying time of the stomach is delayed there is a frequent passage through the pylorus of small amounts of stomach content sufficient to stimulate the duodenum. Furthermore, in certain animals, as in Dog 12, there was a delay of 80 per cent in the emptying time of the gall bladder, and a delay of only 28 per cent in the emptying time of the stomach.

In the past, various authors have called attention to the association of the gall-bladder disease with pathology elsewhere in the gastro-intestinal tract or within the peritoneal cavity. The more recent work of Birch, and Boyden (2) demonstrated a delay of the emptying time of the gall bladder following faradic stimulation of other portions of the gastro-

intestinal tract. The work here reported likewise indicates that the emptying of the gall bladder is under the control of reflex pathways associated with other portions of the gastro-intestinal tract and it is probable that dysfunction and stasis of the gall bladder may be due in part to inhibitory reflexes arising from chronically diseased portions of the gastro-intestinal tract. Likewise certain cases of postoperative vomiting may be explained as the result of gastric dysfunction by means of these reflex pathways.

SUMMARY

1. The effect of remote stimulation of the peritoneum on the emptying time of the stomach and gall bladder has been studied in dogs by means of roentgenograms.

2. Such stimulation results in a delay in the emptying time of both the stomach and gall bladder.

3. It is suggested that certain types of gastric and gall-bladder dysfunction and stasis may be explained on the basis of these reflex pathways.

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THE ABSORPTION FROM TRAUMATIZED MUSCLES[1]

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THE toxæmia theory of shock assumes that an absorption of toxic products from the injured area is responsible for the diminution of blood volume and the decrease in blood pressure. The experiments described in this paper were undertaken to determine the relative absorptive powers of traumatized and normal tissues. Underhill, Kapsinow, and Fisk, in studying burns found that, "after a short latent period absorption from the burned area is much slower than it is under normal conditions."

The studies were performed on dogs. They were deeply anæsthetized by sodium barbital (0.3 gram per kilogram of body weight) that was given intravenously. The animals gave no evidence of pain during the experiment and were killed at its completion. Muscle injury was produced by striking the thigh repeated hard blows with a hammer. The blows were not directed over the femoral vessels. The skin was not torn and the femur was not broken. The duration of the traumatization was approximately 5 minutes. Thirty minutes after the traumatization was terminated, the phthalein or strychnine was injected into the injured muscle. The arterial blood pressure was recorded throughout the experiments.

Experiments with phenolsulphonephthalein. The studies with phthalein included three groups of experiments: (1) those in which the dye was injected into the muscle of the anterior abdominal wall of normal dogs; (2) those in which the dye was injected into the anterior abdominal wall of dogs which had had one extremity traumatized; and (3) those in which the dye was injected into the injured muscle of a traumatized extremity. A catheter was placed in the bladder at the beginning of the experiment, and the bladder was emptied. Each animal received 12 milligrams of phthalein shortly after 350 cubic centimeters of tap water had been introduced by stomach tube. The phthalein excretion was determined at hourly intervals for the first 6 hours following its introduction. Further determinations were usually performed 6 and 18 hours later. The results of these experiments are given in Table I.

From this table it is to be seen that there was very little variation in the dye elimination by the different normal animals. Most of the dye had been absorbed and excreted 4 hours following its injection. The average amount of phthalein recovered in the urine during the entire course of these experiments on normal dogs was 94.5 per cent of that injected. The percentage of phthalein recovered from the urine of dogs which had one extremity traumatized and the dye injected into the anterior abdominal wall varied from 80 to 97, the average being 87.5 per cent. The elimination of the dye was slower in these experiments than in those in which no trauma was carried out. A greater amount of the dye was recovered in the second hour than in the first.

When the dye was injected into the center of the traumatized area a smaller proportion of it was recovered. The average elimination was 53.8 per cent of that injected. Also the rate of elimination was considerably slower.

From these experiments it is evident that the absorption of the dye from injured muscle, as compared with that from normal muscle, is markedly diminished.

Experiments with strychnine. The time of the onset of convulsions, the character of the convulsions, and the effects on the animals were noted in 3 types of experiments: (1) those in which strychnine was injected into the anterior abdominal wall of normal dogs; (2) those in which the drug was injected into the anterior abdominal wall of dogs which had had an extremity traumatized; and (3) those in which strychnine was injected into the injured muscle of a traumatized extremity. The amount of strychnine that was injected in all experiments was 10 milligrams per kilogram of body weight. The results of these experiments are given in Table II.

It is to be seen in this table that five normal anæsthetized dogs received an injection of

[1]From the Department of Surgery of Vanderbilt University. Aided by a grant from the Fluid Research Fund of the Rockefeller Foundation.

TABLE I.—INJECTIONS OF PHENOLSULPHONEPHTHALEIN

Exp. No.	B. P. mm. Hg. and phthalein per cent	Hours following injection								Total percent phthalein recovered
		1	2	3	4	5	6	12	24	
Normal dogs. Dye injected into anterior abdominal wall.										
1	B. P.	158	154	158	148					
	Phthalein	50	35	8	3					96
2	B. P.	120	114	124	128		107	108	92	
	Phthalein	35	25	18	10		2	3		93
3	B. P.	124	126	106	118		94			
	Phthalein	28	30	19	13		8			98
4	B. P.	160	160	160						
	Phthalein	50	28	11	3					92
5	B. P.	111	108	118	129		117			
	Phthalein	30	30	19	8		5			92
Average total elimination of phthalein										94.5
Traumatized dogs. Dye injected into anterior abdominal wall										
1	B. P.	106	115	110	108	94	84	Died		
	Phthalein	14	27	20	14	5				80
2	B. P.	104	106	106	108	96	96	70		
	Phthalein	8	21	20	18	12	6	10		95
3	B. P.	124	130	128	122	118	110	76		
	Phthalein	7	18	21	19	10	4	8		87
4	B. P.	50	86	76	84	80	72			
	Phthalein	4	9	23	20	11	6	13		86
5	B. P.	106	108	110	112	112	100	96	64	
	Phthalein	19	26	32	13	3	2	2		97
6	B. P.	142	135	140	138	141				
	Phthalein	8	16	21	16	12	6	2		81
Average total elimination of phthalein										87.5
Traumatized dogs. Dye injected into center of injured area										
1	B. P.	103	108	115	118	106	108	88		
	Phthalein	5	12	12	10	9	7	9		64
2	B. P.	120	116	117	110	116	110	90		
	Phthalein	2	12	10	8	7	2	11		52
3	B. P.	120	126	124	112	136	140			
	Phthalein	3	17	10	4	10	10		10	64
4	B. P.	112	108	112	110	114	116	88		
	Phthalein	3	11	13	11	11	10	3		62
5	B. P.	120	130	96	76	86				
	Phthalein	5	5	2	2			13		27
Average total elimination of phthalein										53.8

TABLE II.—INJECTION OF STRYCHNINE

Dosage 10 mgms. per kilogram of body weight

Exp. No.	Time between injection and first convulsion	Character of convulsion	General remarks
		Normal dogs. Strychnine injected into anterior abdominal wall	
1	7 min.	Very severe	Dog died 1°45′ after injection during a severe convulsion. B. P. 118 mm. Hg. just before fatal convulsion.
2	21 min.	Severe	Survived. Dog killed 5 hours after injection
3	10 min.	Very severe	Dog died 1°15′ after injection during a severe convulsion
4	15 min.	Severe	Dog survived. Killed 4 hours after injection
5	7 min.	Very severe	Dog died during severe convulsion 36 minutes after injection
		Traumatized dogs. Strychnine injected into anterior abdominal wall	
1	20 min.	Severe. Short duration	Died 3°10′ after injection. Death not preceded by convulsion
2	20 min.	Moderately severe	Died 3°12′ after injection, probably of shock
3	6 min.	Severe	Died during severe convulsion 27 minutes after injection. B. P. was 110 mm. Hg. just before fatal convulsion
4	16 min.	Severe	Died 2°26′ after injection during a convulsion
5	11 min.	Severe	Died 50 minutes after injection
		Traumatized dogs. Strychnine injected into injured area	
1	No convulsions		Gradual fall of B. P. Died of shock 54 minutes after injection
2	2 hours, 30 min.	Few mild jerks	Died of shock 16 hours after injection
3	3 hrs.	One mild convulsion	Died of shock 5 hrs. after injection
4	1 hr. 30 min.	9 mild convulsions	Gradual fall of B. P. Died 2°5′ after injection, probably of shock
5	1 hr. 10 min.	6 mild convulsions	Gradual fall of B. P. Died 3 hrs. after injection, probably of shock

strychnine into the anterior abdominal wall. The time between the injection and the first convulsion varied from 7 to 21 minutes in the different experiments. Three of the animals died after having severe convulsions. The 2 remaining dogs had severe convulsions but survived.

In 5 experiments one of the posterior extremities was traumatized and strychnine was injected into the anterior abdominal wall. The onset of convulsions varied from 6 to 20 minutes following the injection. The convulsions were quite severe in four of the five experiments. All the animals died. In two experiments, death occurred during a severe convulsion. Death was probably due to the trauma in 2 animals which lived for more than 3 hours following the injection. There were no convulsions for a considerable period preceding the death of these 2 animals. In the remaining experiment in which the animal lived 50 minutes, death occurred 10 minutes following a severe convulsion and it was not known whether the animal died as a result of the administration of the strychnine, or the trauma, or both.

No severe convulsions were produced by the injection of strychnine in the 5 experiments in which it was introduced into the injured muscle. Four of the animals had mild convulsions. The time separating the injection of strychnine and the onset of convulsions varied from 1 hour and 10 minutes to 3 hours. The animals which had convulsions lived from 2 hours and 5 minutes to 16 hours following the injection of strychnine. Death in all instances was almost certainly due to the trauma and not to the strychnine.

These experiments show that the absorption of strychnine from the anterior abdominal wall is altered very little by trauma to an extremity. On the other hand, strychnine is absorbed very slowly when it is introduced into the traumatized area itself.

SUMMARY

The absorption of phenolsulphonephthalein and of strychnine by deeply anæsthetized dogs has been studied under three experimental conditions: (1) normal dogs in which the injections were made into the anterior abdominal wall; (2) dogs with a traumatized extremity in which the injection was made into the anterior abdominal wall; and (3) dogs with a traumatized extremity in which the injection was made into the injured muscle. There was not a great deal of difference in the absorption of the solutions that were injected into the anterior abdominal wall of normal dogs and of dogs with a traumatized extremity except for a slight delay in the latter group. On the other hand, the absorption of the phenolsulphonephthalein and of the strychnine that was injected into the traumatized area itself was greatly retarded.

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THE CONCEPTION PERIOD IN NORMAL ADULT WOMEN

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THE epoch making work of Aschheim and Zondek has definitely shown that hormonal secretions play a prominent rôle in pregnancy. These hormones are derived from the ovary and the pituitary gland, and bear a direct relationship to ovulation, fecundation, and menstruation. Recent investigation indicates that there are seven distinct hormonal effects from the pituitary gland and two from the ovary. The effects from the pituitary gland are:

1. The anterior lobe.

a. An effect causing ripening of the graafian follicle with the production of folliculin and egg cell (1).

b. An effect which causes growth of the corpus luteum after ovulation (2).

c. An effect which in conjunction with the corpus luteum causes hypertrophy of the mammary glands (3, 5, 11, 13, 18, 24).

2. The posterior lobe.

a. An effect causing uterus stimulation (12, 13, 18).

b. An effect causing expansion of melanophores (35).

c. An effect causing antidiuresis or water retention (32).

d. An effect causing increased blood pressure (9).

The effects from the ovary are:

a. Folliculin which causes hyperæmia of the uterus and tubes in preparation for the egg cell (7).

b. Corpus luteum which produces further growth of uterus and hypertrophy of mammary glands (6, 8).

Ripening of the graafian follicles with the production of folliculin and ovum is brought about by an anterior pituitary hormone. Folliculin causes hyperæmia of the uterus and tubes. When the follicle bursts the corpus luteum spurium is formed and this body in turn causes further growth of the uterus and hypertrophy of the mammary glands. If the egg cell is not fertilized the corpus luteum withers and dies and menstruation takes place. If the fertilized egg is implanted the corpus luteum spurium develops into the corpus luteum gravitatis, which maintains pregnancy and when it begins to wither the posterior lobe hormones re-assert causing rhythmic contractions of the uterus and labor. These reactions are shown by Figures 1 and 2 (13, 14, 15, 30).

Different scientists have shown that the life of the human egg cell is 1 day (18, 24, 34) and that of the sperm cell is 2 to 3 days (18, 24, 36). Also that in a normal regularly menstruating woman with a cycle of 28 to 30 days,

ovulation occurs between the fourteenth and sixteenth days (18, 24), and that 10 days are required for the passage of the egg cell through the fallopian tube (18).

Henle has definitely shown that spermatozoa are able to travel a distance of 1 centimeter in 3 minutes (37). That human spermatozoa may reach the fallopian tube in a very short time after being deposited in the female genitalia, there can be no doubt, as shown by the following case, which we observed:

Mrs. B. M., age 25, i-para; diagnosis, dyspareunia, prolapsed uterus. In this case the last coitus was 65 days previous. Examination of vaginal and cervical secretions did not show the presence of spermatozoa. Copulation was had at 8 a.m.; 2 hours later at laparotomy examination of fallopian tubes revealed the presence of numerous spermatozoa.

If the duration of life of the egg and sperm cell is known, as well as the rate of sperm cell motion, the next question which confronts us is: When is the egg cell liberated?

Knaus, by means of a manometer noted that there was increased uterine pressure following the injection of posterior lobe pituitrin due to uterine contractions and that when corpus luteum was present the uterus did not respond by contractions (36). In this manner he was able to determine the time of ovulation. This he found to be in the 28 day cycle of menstruation on the fourteenth to the sixteenth days before the next menstruation (18, 24). From these facts it is evident that in a 28 day cycle the corpus luteum spurium functions for about 14 days, when implantation of a fertilized egg occurs the corpus luteum spurium is changed to corpus luteum gravitatis, or if fertilization and implantation do not occur it withers and dies and menstruation is brought about. On this view pregnancy is not a hit and miss affair, but is regulated by the meeting of the egg and sperm cell before one or the other has withered and died (18, 36).

Ogino, of Japan, studied this question by examining the coitus in relation to ovulation and noting its ability to fecundate. He arrived at the following conclusions:

1. For women regularly menstruating every 28 days the period of time the human sperm cell was able to impregnate the ovum was the 8 day period lying between the twelfth and the nineteenth day before the next menstruation or in other words, between the tenth and the seventeenth day after menstruation had started, other days being physiologically sterile.

2. If the cycle is longer or shorter than 28 days the period of conception is moved so many days ahead or behind.

3. For those women who do not have a greater variation in the menstrual cycle than 10 days a formula for the period of conception could be stated as follows:

Beginning of conception is 10 plus cycle of minimum days—28.

End of conception period is 17 plus cycle of maximum days—28.

4. In computing the period of conception of any woman 12 menstrual cycles should be known, noting the maximum and minimum length of time of each. If the menstrual cycle should vary more than 10 days, then the formula is still theoretically correct, but of not much practical value (31).

Knaus, of Austria, working independently, arrived at similar conclusions, but elaborated them more fully as follows:

1. For women with a regular menstrual cycle of 26 days, conception possibilities are limited to the time from the ninth to the thirteenth days, inclusive.

2. For women with a regular menstrual cycle of 27 days, conception possibilities are limited to the time from the tenth to the fourteenth days, inclusive.

3. For women with a regular menstrual cycle of 28 days, conception possibilities are limited to the time from the eleventh to the fifteenth days, inclusive.

4. For women with a regular menstrual cycle of 30 days, conception possibilities are limited to the time from the thirteenth to the seventeenth days, inclusive.

5. For women with a regular menstrual cycle of 34 days, conception possibilities are limited to the time from the seventeenth to the twenty-first days, inclusive.

6. For women with a regular menstrual cycle of 28 to 30 days, conception possibilities are limited to the time from the eleventh to the seventeenth days, inclusive, with the maximum of same at the fourteenth to the sixteenth days.

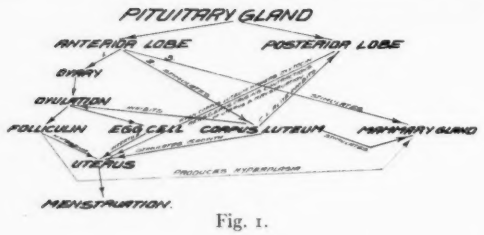


Fig. 1.

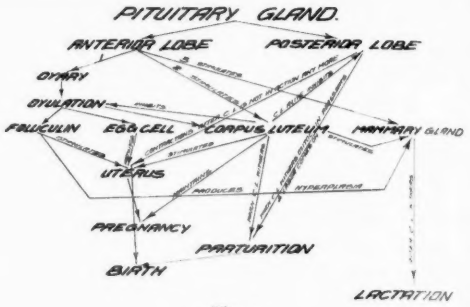


Fig. 2.

7. For women with a regular menstrual cycle of 26 to 30 days, conception possibilities are limited to the time from the ninth to the seventeenth days, inclusive, of the menstrual cycle.

For menstrual cycles of other variations, the conception period may be computed in the same manner as stated above. These calculations being true only for normal, healthy women with regular variations in the cycle as stated above (16, 19 to 29).

Ogino established the time of ovulation in an empirical manner during the course of laparotomies on women. He has a 5 day ovulation period in a constant menstrual cycle.

Knaus determined the time of ovulation by measuring the uterine contractions by means of a manometer. He has a 2 day ovulation period in a constant menstrual cycle. It seems to us that Knaus' method is more definite and precise; therefore, we follow the doctrine of Knaus.

Based upon this initial research we decided to study this question by examining the coitus at various times to determine its ability to fecundate. Our material was chosen from 87 apparently normal couples including 8 nationalities and 725 copulations. Where pregnancy was thought to have occurred it was checked by the modified Aschheim-Zondek test on rabbits.

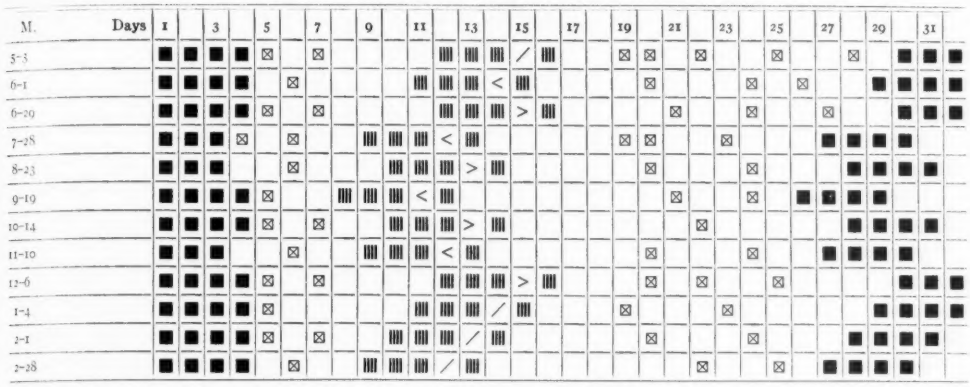
Our observations are as follows:

CASE 1. E. B., aged 36 years. Menstruation commenced at the age of 13, was of regular cycle, 28 to 30 days; duration 4 to 5 days. Patient was married at the age of 16 on the thirteenth day after previous menstruation; result pregnancy. For 5 years after birth of child, not desiring more children, various contraceptive methods as suppositories, douche powders, and pessaries were used. During the fifth year, while wearing a pessary, she became pregnant and aborted at the second month. At this time she was informed by a friend to abstain from coitus between the tenth and twentieth day of her menstrual cycle. This she practiced successfully for 13 years without the use of any contraceptive measures whatever, except accurately noting the dates on the calendar as well as duration of each cycle as the months went by. At the beginning of her fourteenth year of this procedure, she was informed that she must not figure from the first day of menstruation, but from the last. She accordingly changed her system. The next and only coitus occurred on the fourteenth day from the beginning of the last menstrual period. Result: amenorrhœa, of 2 months. On the third day after the second missed cycle, the Aschheim-Zondek test revealed pregnancy. Ten days later, by self-induced means, she aborted a 2 months fetus. In this case the cohabitation date lies within the period of conception for her.

CASE 2. F. E., aged 28 years. Menstruation began at the age of 14 years, was occurring every 26 to 28 days, duration 4 days. She was married at the age of 21, the date being about halfway between two menstruations. Result, pregnancy. Following birth of child she developed a painful right ovary. Menstruation became profuse, 5 to 6 days in duration, varying from 26 to 34 days. She was advised by her physician that another pregnancy might result in an operation being necessary so she used various contraceptive measures for 6 years. At this time, feeling that her procedure was correct, she adopted a son. Later she was advised that contraceptives were injurious and unnecessary, if she would abstain from intercourse between the eleventh to the seventeenth days of menstrual cycle. The previous 4 periods were as follows: 26, 30, 28, and 32 days in duration. The only cohabitation during the month was on the nineteenth day after the beginning of the last menstruation. Result: amenorrhœa. The Aschheim-Zondek test proved the existence of pregnancy. This day lies within the dates of conception possibilities for her.

CASE 3. A. A., aged 25 years. Menstrual cycle varied from 29 to 33 days, duration 4 days. Last 4 menstruations were as follows: January 27, 1932, February 29, 1932, March 29, 1932, April 30, 1932. Only cohabitation on May 16, 1932, then amenorrhœa. The Aschheim-Zondek test on June 12, 1932, proved the existence of pregnancy. The cohabita-

TABLE I.—CASE 1, A. F.



■ Menstruation. ▥ Period of conception. ⁄ < Maximum period of conception. ⊠ Cohabitation.

tion date in this case falls within the conception period for this woman.

CASE 4. A. R., aged 26 years. Menstrual cycle was 27 to 33 days, duration, 4 days. The last 5 menstruations are as follows: January 2, 1932, February 3, 1932, March 1, 1932, April 3, 1932, and May 4, 1932. Only cohabitation was on May 18, 1932. The next menstruation due to occur during the first week in June failed to materialize by June 16, on which date the Aschheim-Zondek test proved the existence of pregnancy. The cohabitation here is within the period of conception possibilities for this cycle.

CASE 5. A. N., aged 42 years, vi-para; 3 abortions. Menstrual cycle was 30 to 31 days. Last two menstruations were as follows: January 10, 1932, and February 10, 1932. The only coitus was on February 25, 1932. The following day her husband left home to seek work in a distant state and was gone for 4 months. This woman did not menstruate during the next 3 months. Being in ill health and believing that she was entering upon the climacteric she consulted a physician. The Aschheim-Zondek test proved pregnancy was the cause of amenorrhœa.

CASE 6. W. E., aged 22 years, regular 26 to 28 day cycle menstruation. Confined on August 14, 1931. First menstruation postpartum was December 25, 1931. Next four as follows: January 22, 1932, February 17, 1932, March 16, 1932, and April 14, 1932. One coitus occurred on April 30, 1932. On May 14, 1932, Aschheim-Zondek test was positive for pregnancy.

CASE 7. E. A., aged 21 years. Regular menstrual cycle 26 to 30 days. Last menstruation was on April 6, 1932. Cohabitation was on April 22, 1932. On June 11, 1932, Aschheim-Zondek test was positive for pregnancy.

CASE 8. A. B., aged 40 years, viii-para; menstruation every 26 to 27 days; duration 2 to 3 days. Last menstruation on August 10, 1931; cohabitation on August 21, 1931. On September 18, 1931, Aschheim-Zondek test was positive for pregnancy. In her case the conception date lies on the second day of the period of conception for her.

CASE 9. H. L., aged 35 years, no children; regular menstrual cycle of 30 days, duration 5 days. Last period was February 29, 1932, cohabitation March 13, 1932. Result, pregnancy.

CASE 10. H. C., aged 21 years, on August 27, 1925 was confined. This woman believed that as long as she was nursing a child and did not menstruate that she could not become pregnant. Feeling secure in this belief no contraceptive measures were used. Eight months after her confinement, no menstruation having appeared as yet on October 12, 1926, she consulted a physician and pregnancy was diagnosed. She was again confined. In this case no menstruation occurred between the birth of the first child and the birth of the second child.

COHABITATIONS REGULATED BY TIME WHICH DID NOT RESULT IN PREGNANCY

CASE 1. A. F., aged 27 years, i-para. This woman used the premenstrual and postmenstrual period of sterility for cohabitation. The details are shown in Table I.

In this case there were 48 cohabitations which did not result in pregnancy.

Eighty-seven cases consisting of 12 different menstrual cycles and 8 nationalities were studied for the period of physiological sterility. The details of this study are shown in Tables II and III.

Cohabitations before and after menstruations total 725 and not a single cohabitation of these two groups resulted in pregnancy.

TABLE II

Cases	Cycle	Months	Days before next menses													Total
			13	12	11	10	9	8	7	6	5	4	3	2	1	
3	26–27	4							2	3	2	1	6	6	4	24
5	26–28	6						1	2	7		16		9	14	49
9	26–30	3							6	9	12			14	8	49
3	26–34	4								2	4	1	5	3	7	22
6	27–33	5								3	9	4	6	20	5	47
23	28–30	2			4			6			9		8		12	39
1	28–34	5											2	1		3
2	28–36	2									8	4	1	5	6	24
7	29–33	3								8		7	5		9	29
1	29–30	5			1	2		1	3	2		1	2		1	13
12	30	2			2		4		2			7		3	4	22
15	30–31	2			7		10		4	7	1		9		12	50
87					14	2	14	8	19	41	45	41	44	61	82	371

TABLE III

Cases	Cycle	Months	Days after menstruation												Total
			1	2	3	4	5	6	7	8	9	10	11	12	
3	26–27	4	4	1	3	4									12
5	26–28	6	8	7	18	14									47
9	26–30	3	14	8	14	12									48
3	26–34	4	11	2	6	5									24
6	27–33	5	10	8	12	10									40
23	28–30	2	38	4	12	10	7								71
1	28–34	5	2		3		4	1							10
2	28–36	2	1		2	2									5
1	29–30	5	3		1		1	1							6
7	29–33	3	3	12	1	9	6								31
12	30	2	10	3		12	4								29
15	30–31	2	12	3		12	4								31
87			116	48	72	90	26	2							354

SUMMARY

The anterior lobe secretion motivates the ovary. The corpus luteum inhibits the posterior lobe secretion and maintains pregnancy. When the corpus luteum withers the oxytoxic principle of the posterior lobe secretion asserts itself and labor is brought about. Fecundation is only possible when the sperm cell is properly timed to meet the egg cell.

CONCLUSIONS

1. Hormones play a major rôle in pregnancy.

2. The sperm and egg cells detached from their respective breeding places have a very limited time to live. For the egg cell it is not longer than 1 day. For the sperm cell it is 2 to 3 days.

3. Every normal regularly menstruating woman has a definite ovulation period.

4. Every normal regularly menstruating woman has a definite period of physiological sterility and a definite period of fertility in each cycle.

5. Cohabitation must be properly timed with ovulation if pregnancy is to result.

6. Pregnancy may be brought about or avoided at will by the observation of these two periods of time.

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THE INTERRELATIONSHIP BETWEEN OVARIAN FOLLICLE CYSTS, HYPERPLASIA OF THE ENDOMETRIUM, AND FIBROMYOMATA

A Possible Etiology of Uterine Fibroids

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UTERINE fibroids, because they are the most common of all pelvic neoplasms, should command the interest of every gynecologist. Various theories of their origin have been propounded, but no accepted explanation has yet been advanced, and their true histogenesis will probably remain a mystery until the cause of neoplasms in general is discovered. However, recent additions to our knowledge concerning the ovarian and pituitary hormones now offer a definite approach to the origin and development of these benign tumors. Past research into the pelvic field has revealed the interrelationship of ovarian follicle cysts and hyperplasia of the endometrium, and although in the evidence brought forth, there exists numerous instances of the association of fibromyomata with these two conditions, the action of ovarian dysfunction on the myometrium has been little investigated or commented upon. I believe that the existence of an etiological relationship between hyperplasia of the endometrium, ovarian follicle cysts, and fibromyomata is highly probable, and the results of my investigations have prompted the writing of this paper.

The histogenesis of fibroids is not definitely known, and lends itself to the explanations given to neoplasms in general: an origin from embryonic rests (Conheim), a product of connective metaplasia, etc. McCallum is one of the few advocates of Virchow's uterine muscular origin theory and he contends that this belief is substantiated by the fact that myomata relax and soften during pregnancy and recover their hardness after confinement. Opitz suggests metaplasia of connective tissue, since both uterine muscle and connective tissue originally develop from the same undifferentiated process of the mesenchyme; continuation or repetition of this metaplastic process must occur to produce fibroids. Roesger is of the opinion that fibroids arise from the walls of the blood vessels, but this belief is not substantiated by Cullen. A relationship between uterine fibroids and the terminal branches of uterine arteries, similar to that found between neuromata and the epineurium, has been suggested; other observers note an inflammatory cause: von Recklinghausen considers wolffian remnants to be important in their origin, while still others believe that the development is to be found in the aberrant muellerian tissue. Ewing is of the opinion that the essential histogenetic factor is an embryonic disturbance in the structure of the uterus, because of the remarkable degree of isolation of the many myomata, their widespread occurrence over the body other than in the uterus, and the presence in many cases of heterotopic inclusions, epithelial, cartilaginous, osseous, fatty, and rhabdomyomatous, clearly point to an embryonic origin.

Numerous cases have been reported which seem to show that heredity may play some part in the etiology of fibroids, although only 21 women in Lynch's series of 683 cases gave an indicative family history. The relative frequency of this type of tumor in negroes suggest the influence of race as a factor. In Charity Hospital, New Orleans, where the annual admission of the white and colored patients is about equal, fibromyomata were noted 9 times as frequently in the colored patients as in the white. Bulloch describes this growth and other fibroid tendencies of the negro as a racial peculiarity, though there is a general impression extant that these growths were unknown among the primitive tribes. Why there should be any relationship between the development of fibroids and the advancing civilization of negro women is difficult to understand, unless, as will be discussed in a subsequent paper, ovarian dys-

function brought on by pelvic infection should play an etiological rôle. However, scientific data are still wanting to confirm definitely that either heredity or race is the cause.

Sterility has long been noted as another factor in the etiology of fibroids, since it is found to be three times as prevalent in association with fibroids as it is under normal conditions. Young and Williams (Lockyer) note 10.5 per cent sterility in all women who have attained the age of 38, while in a large series of cases of fibroids Cullen, Phillips, Olhausen and Lynch found 30 to 33 per cent sterility in the married woman. It is an accepted fact that fibroids occur most frequently in virgins and in absolutely or relatively sterile women. One child sterility is frequently observed, and in Miller's 150 cases of fibroids 50 per cent of the fertile colored women had only 1 child. Lynch and Cullen offer as an explanation of this observation the fact that uterine muscle is primarily designed to respond to pregnancy in all of its various functions and manifestations, and should no pregnancy intervene, this organ responds to a less influential stimulus and hypertrophies in an abnormal fashion, resulting in the development of fibroids. This theory, however, does not offer any explanation of the development of fibroids in a parous woman, nor does it explain their stimulation to rapid growth when associated with pregnancy. Fibroids, because of their size and pressure and the high incidence of associated infection, often cause mechanical sterility. Both sterility and fibromyomata are prone to develop in the infantile type of uterus, as well as from displacements and other uterine defects which often enhance the early termination of the pregnancy by abortion. The essential problem is whether sterility is the cause of fibroids or fibroids the cause of sterility.

In view of the fact that the occurrence of fibroids is generally noted during the childbearing years of woman, menstruation should play an important part in their etiology. On this hypothesis, Sampson offers as an explanation local hyperplasia of the uterine muscle cells, caused by the stimulus of menstrual blood which has acquired access to the myometrium by retrograde flow through the venous sinuses of the endometrium. As proof, the author cites the fact that smooth muscle tissue in contact with heterotopic endometrial tissue, often shows a tendency to grow. The absence of fibroids in the tubes and in the cervix is explained by lack of menstruation in these parts. Sampson suggests that the cause of the greater frequency of fibroids in the human female over that in the lower animals is due to the monthly periods in woman, since the animal cycle is not true menstruation. Moench points out, however, that menstruation does occur in the ape, and that fibroids are relatively unknown in this animal.

There is a general clinical impression that glandular dysfunction is associated with fibroids. Polak's observation of unbalanced glandular patients lead him to believe that the hyperpituitary type of woman, who begins her menstrual life with an anteverted, anteflexed uterus, and a relative large uterine body, is prone to develop fibroids. He has followed 100 or more women over a 10 to 15 year period and has "watched them grow fibroids." Fibroids often develop in the subthyroid and the subpituitary types with anteflexed retroverted uteri, and with clinical symptoms of glandular hypoplasia, primary dysmenorrhœa, and sterility. On the other hand, women of perfect endocrine balance seldom grow fibroids even though pregnancy is a frequent occurrence, with the uterus passing through alternate periods of hypertrophy and involution. In reviewing 683 cases of fibroids, Lynch observed thyroid involvement, adenoma, hyperthyroidism, or simple goiter, singularly or in some combination, in 106 patients (15.5 per cent). In 394 cases of large fibroids, the abnormality of the thyroid was involved in 77 patients (19.5 per cent).

Ovarian activity has generally been considered a factor in fibroid development because of its occurrence during woman's functional years, and while this consideration has been based only on clinical observations and general impressions, its existence evidences a trend of thought along the line of ovarian hormone influence on the uterus. Schroeder and R. Meyer, in Germany, and

Novak, Fluhmann, and Graves in this country have brought forth convincing evidence to prove the relationship between ovarian follicle hormone and hyperplasia of the endometrium. This pathological condition manifests itself as irregular uterine bleeding which is most frequently noted clinically at the two extremes of woman's functional years, and histologically is described as containing a characteristic lack of uniformity of the glandular elements embedded in a varying amount of densely packed stromal proliferation, the so-called "Swiss cheese pattern." Because of its microscopic resemblance to hypertrophy of the basal layer of the endometrium, the hypothesis is logical that its structure results from overgrowth of this layer at the expense of the superficial layers whose growth is governed by the hormone of the corpus luteum.

Schroeder had an opportunity of examining the uterus and both ovaries in 62 cases of hyperplasia of the endometrium. In 53 instances the ovaries contained 1 or more small cysts, lined with well preserved granulosa and theca layers; in a few instances, the ovum was demonstrated in the granulosa cells. In the 9 remaining cases the follicles were undergoing degeneration, and one early corpus luteum was seen, but was thought to have been ruptured a few days previously by bimanual examination. From these observations, Schroeder proposed the theory of "pathological persistence of a ripening follicle" as the cause of hyperplasia of the endometrium. He contends that the ovum does not die and the follicle, unruptured, continues to function, resulting in excess secretion of the follicle hormone. R. Meyer substantiated the evidence of the absence of the corpus luteum formation in hyperplasia, but he noted large cysts of the ovaries caused from apparent follicle atresia, in addition to the many normal granulosa cell cysts. The walls of the larger cysts presented an unusual hypertrophy of the theca cells. Theorizing from these observations, Meyer advanced the idea that the ovum dies prematurely, due to some unknown inherent weakness, and in consequence the follicle does not reach complete maturity, nor does it rupture, but undergoes atresia at an earlier period. Immediately another ripening follicle appears, and the process is repeated, thus maintaining continuous ovarian follicle stimulation to the endometrium. Even though the explanations of Schroeder and Meyer of the methods of production of the follicular hormone differ, they completely agree that continuous stimulation by it in the absence of corpus luteum influence is the cause of hyperplasia of the endometrium.

In a smaller series of cases Fluhmann, Graves, and Novak generally support this hypothesis as the cause of endometrial hyperplasia as attested by the following facts: (1) it is observed only during woman's functional years; (2) it occurs at the two extremes of woman's menstrual life, when the ovarian cycle tends not to follow its normal rhythm, since it is just beginning or ending; (3) there is no evidence of inflammatory origin since it occurs in very young girls; (4) the bleeding resulting from it is checked by removing the ovaries and destroying ovarian function by X-ray; (5) curettage gives only temporary relief, suggesting that the underlying cause has not been reached; (6) the presence of follicle cysts is constantly found and excess follicle hormone content is noted in the blood at such periods; (7) estrin has been proved experimentally to be a growth hormone to endometrial glands and stroma, and hyperplasia presents similar histological characteristics; (8) it found after the menopause from granulosa cell tumors which give rise to excess estrin, or hyperestrinism (Graves) in the blood; (9) the absence of corpora lutea precludes the formation of progestin; (10) and the lack of progestin, the corpus luteum hormone, is confirmed by the absence of endometrial secretory changes, normally produced by this hormone.

Since the discovery of the "motor control" of the anterior pituitary gland over the ovarian function, Novak and Burch have suggested the anterior hypophysis, acting through the ovary, as being the fundamental etiological factor of hyperplasia of the endometrium. According to Novak the interrelationship of the anterior hypophysis is chiefly responsible for the alternating phases of the long continued amenorrhœa and persistent bleeding seen in the familiar type of

adiposogenital dystrophy. The participation of this gland as an etiological factor is further suggested by the cases of functional bleeding occurring after full term pregnancies or miscarriages, since it is well known that the anterior pituitary gland undergoes marked hypertrophy during gestation. Novak has obtained splendid clinical results from the treatment of functional bleeding by the administration of anterior pituitary hormone, while Burch has demonstrated experimentally that there is a definite cyclic variation in the capacity of the anterior lobe to produce ovulation.

From the above evidence it seems legitimate to conclude that hyperplasia of the endometrium is the result of the unopposed and continued action of the ovarian follicle hormone in the absence of the corpus luteum influence. If this be true, the reverse ought to hold, namely, when endometrial hyperplasia is found in curettings, the diagnosis of ovarian follicle cysts can be assumed. Since the uterus as a whole is involved in the reproductive process, it seems logical to deduce that the action of estrin is not limited solely to the endometrium, but that the myometrium is also involved, especially if there be pathological stimulation to this myometrial tissue at the same time that the endometrium is abnormally stimulated to hyperplastic formation.

Novak has observed, in evidence presented but uncommented upon, the association of ovarian follicle cysts, hyperplasia of the endometrium, and fibromyomatous changes in the myometrium. In 32 uteri with hyperplastic characteristics of the endometrium, he found myomatous involvement of the myometrium in 23 cases (71.8 per cent); in 15 cases the myomata were alone, 5 were combined with adenomyomata, and in 3 cases the latter growth alone was present. Turco comments upon the cystic degeneration of the ovaries in 11 cases of fibroids, but concludes that it is difficult to tell whether degeneration of the ovaries was the result or cause of the fibromyomata. Graves, in 237 cases of hyperplasia treated with radium, noted fibroids clinically in 50 per cent. In 25 cases of fibroids in which hysterectomy and bilateral oophorectomy were done, he found 11 cases of hyperplasia. In the same communication this author discussed uterine bleeding with and without fibroid association; his conclusion was that abnormal uterine bleeding associated with fibroids is identical in etiology and character with the so-called idiopathic or functional uterine hæmorrhage, characterized by the "Swiss cheese pattern" of the endometrium, except in cases of pedunculated, degenerating, and submucous fibroids, and exposed adenomyomatous growths.

Since the rate of growth of fibromyomata is not exceedingly rapid except in pregnancy, malignancy, and possibly in youth, it would seem legitimate to assume that if these growths are the results of the unopposed estrin stimulation of the myometrium, their appearance would be slower than the hyperplastic endometrial changes. Hence it might be concluded that the unopposed action of estrin on the uterus results: (1) in immediate endometrial changes, characterized by hyperplasia, and (2) in more latent myometrial pathology in the nature of fibromyomatous growths.

With this hypothesis as a basis, an analysis was made of 26 cases of hyperplasia of the endometrium, in which operation was done and diagnosis as such made, and in which a second operation was performed for fibromyomata after an approximate interval of 4 years and 4 months. In addition 124 cases of fibromyomata which were diagnosed microscopically, are offered with the associated ovarian and endometrial findings as presenting added evidence in support of a cause and effect relationship, and suggesting a possible factor in the development of uterine fibroids.

I. In the first group of 26 cases of hyperplasia of the endometrium a curettage was performed, and in no instance was a fibromyoma determined clinically or grossly at the time of this operation, even though the abdomen was opened in 13 cases (50 per cent). After varying intervals all 26 patients were operated upon again because of uterine fibroids, and the findings of the ovaries, endometrium, and myometrium are offered (Table I).

TABLE I.—ANALYSIS OF TWENTY-SIX CASES

	Cases
Age in years	
20 to 29	4
30 to 34	10*
35 to 39	9*
40 to 44	2
45 to 49	1
Total	26

*Age group 30 to 39 represents 73 per cent of cases.

Social status	
Married	21
Single	5
Fertile	15
Sterile	6
Miscarriage, but no full term pregnancy	3
Symptoms	
First operation	
Menorrhagia	13
Metrorrhagia	6
Dysmenorrhœa	7
Second operation	
Menorrhagia	16
Metrorrhagia	3
Dysmenorrhœa	9
Abdominal mass	5
Nervous, irritable	5
Amenorrhœa after radium	2*
No effects from radium	4
Pregnancy after dilatation and curettage	2

*Lasted 3 and 6 months.

Type of operation	
Dilatation and curettage	29*
Application of radium	6†
Suspension of uterus	3‡
Appendectomy	4‡
Unilateral salpingo-oophorectomy	5‡
Bilateral salpingectomy	1‡

*In 1 patient dilatation and curettage was done twice, in another three times.
†Number of hours undetermined.
‡Abdomen opened in 13 cases, 50 per cent of total.

Condition of ovaries at first operation	
Diagnosed microscopically as cystic	5
Diagnosed operatively as cystic	5
Not mentioned at operation	3
Curettings	
Abundant	4
Moderate amount	8
Small amount	4
Polypoid	4
Not mentioned	8
Time interval between operations	
Longest	13 years, 2 months
Average	4 years, 4 months
Shortest	1 year, 2 months
Type of second operation	
Hysterectomy	26
Bilateral salpingo-oophorectomy	13
Removal of all ovarian tissue	5
Unilateral salpingo-oophorectomy	8
Condition of myometrium	
Fibromyomatous	20
Hyperplastic	6
Fibrotic	5
Malignant degeneration	1
Adenomyomatous	1
Normal	11
Metritis	1
Bicornuate uterus	1
Condition of endometrium	
Hyperplastic	24
Premenstrual	2
Ovaries	
Both examined	13*
All ovarian tissue examined	5*
Only 1 ovary examined	8

*18 cases, 69.2 per cent.

Condition of ovaries at second operation	
Follicle cysts	20
Corpus luteum	
Mature	2
Degenerating	5
Absent	19
Miscellaneous	
Salpingitis	11*
Adhesions	14*
Endometrial transplants	7†

*96 per cent.
†27 per cent.

The age limits were well within woman's functional years, 30 to 39 years accounting for 73 per cent of all patients, the average being 35 plus years. The symptoms between the first and second operations offer an interesting comparison, the outstanding feature of which is an increase of complaints. Menorrhagia and dysmenorrhœa were more frequent after the first operation while metrorrhagia decreased. An abdominal mass appeared in 5 instances, while nervousness in the form of irritability became a complaint in a similar number of cases. Radium caused a temporary amenorrhœa in 2 cases for 3 and 6 months, respectively, but was non-beneficial in 4 cases. Pregnancy occurred in 2 women after the initial curettage. The interval between the first and second operation averaged $4^{1}/_{3}$ years, with limits of $1^{1}/_{6}$ years to $13^{1}/_{6}$ years. Twenty-nine curettages were performed, including 2 on 1 patient and 3 on another. The abdomen was opened at the first operation in 13 cases (50 per cent), and in 5 patients the ovaries were diagnosed microscopically as containing follicle cysts. In an equal number of cases the

operator noted the same condition grossly, and punctured the multiple cysts with a needle. No mention of the operative condition of the ovaries could be found in the operative notes of 3 patients whose ovaries were not disturbed. The amount of curettements was described in 18 instances, but since many different doctors performed the 29 curettages, the description of the curettements naturally varies with the individual operator.

The uterus was removed in every instance at the second operation. Bilateral salpingo-oophorectomy was performed in 13 cases, while all the remaining ovarian tissue was excised in 5, a total of 69.2 per cent. One ovary was left *in situ* in 8 cases. Multiple fibroids were observed in every case, and in general the longer the interval between the operations the larger the fibroids. The myometrium was normal in 11 cases (42.3 per cent) even though fibroids were present in the walls. Hypertrophy of the myometrium was noted in 6 instances (23.3 per cent), and fibrosis i.e., increased connective tissue, in 5 cases (19.2 per cent). The endometrium was either hyperplastic or polypoid in 24 cases (92.3 per cent); the premenstrual, pregestational stage was observed in 2 instances, associated in each case with a developing corpus luteum, and interestingly enough it occurred in the 2 patients who had borne children after the initial curettage for hyperplasia of the endometrium. The fibroid tumors in these 2 cases were multiple but small.

Unless both ovaries or the total ovarian tissue are studied in their entirety, it is unwise to draw conclusions concerning the presence or absence of the corpus luteum, since its absence is so importantly related to hyperplasia of the endometrium. In 18 cases (69.2 per cent), both ovaries, or the total remaining ovarian tissue, were studied. In 8 cases (30.8 per cent), in which only 1 ovary was available for study, 2 corpora lutea were observed in the developmental stage, and in each case the secretory phase of the endometrial cycle was associated. In 24 cases (92.3 per cent) no mature corpus luteum could be found, while old degenerating luteal cysts were observed in 5 instances. Follicle cysts of the ovaries were present in all 26 cases including those in which the corpora lutea were found. Any explanation I can offer of the presence of follicle cysts in association with a developing corpus luteum must be in the nature of an hypothesis. That hyperplasia of the endometrium is not always a permanent condition has been observed frequently in young girls, many of whom subsequently bear children; yet its persistence is noted as long as follicle cysts are found in the ovary. However, when menstruation begins to return to normal, ovulation, with the usual subsequent corpus luteum formation, must occur, and at such periods, the change from abnormal functional bleeding over to normal menstruation, the existence of both follicle cysts and corpus luteum might be observed.

In 25 cases (96.1 per cent) salpingitis, or adhesions from previous operations, or endometrial transplants were noted involving the ovaries. The importance of this finding as a possible etiological factor in follicle cyst formation with subsequent ovarian dysfunction, is not to be minimized. The endometrial transplants, mainly to the ovaries (71.4 per cent), were noted in 7 cases (27 per cent). The rather high percentage of this condition associated with hyperplasia of the endometrium and fibroids, as compared with other gynecological conditions in general, is noted as a possible etiological factor of endometriosis.

These 26 cases of hyperplasia of the endometrium on which a second operation was performed on an average of 4⅓ years later for myomatous growths of the uterus are convincing evidence of a cause and effect relationship of the prolonged and unopposed action of estrin on the myometrium, and the development of fibromyomata.

II. A second group of 83 patients on whom hysterectomy was performed for fibroids also supports the hypothesis of the existence of an interrelationship between ovarian follicle cysts, hyperplasia of the endometrium, and myomatous growths of the myometrium (Table II).

Even though both ovaries, or the total ovarian tissue, were available for study in only 50 per cent of the cases, follicle cysts were found in every instance, while no mature

TABLE II.—ANALYSIS OF EIGHTY-THREE CASES

	Cases
Age in years	
20 to 29	6
30 to 34	14
35 to 39	21
40 to 44	21
45 to 56	21
Total	83
Limits—27 and 56 years. 9 women were over 50 years of age.	
Married	70
Single	13
Fertile	42
Sterile	12
Miscarriage, all in parous women	10
Undetermined from histories	16
Menstrual history	
Menorrhagia	68
Metrorrhagia	10
Dysmenorrhœa	11
Irritable	6
Thyroid involvement	1
Family history of fibroids	3
Type of operation	
Hysterectomy	83
Bilateral salpingo-oophorectomy	33
Unilateral salpingo-oophorectomy	50
Condition of myometrium	
Fibroids	83
Hyperplastic	26
Fibrotic	17
Adenomyomatous	4
Carcinomatous	1
Sclerotic vessels	2
Metritic	2
Normal	35
Condition of endometrium	
Hyperplastic	83
Carcinomatous	1
Ovaries	
Both ovaries examined	33*
All ovarian tissue examined	9*
Only 1 ovary examined	41
*50.6 per cent of cases	
Condition of ovaries	
Follicle cysts	83
Corpus luteum	
Absent	73
Degenerating	10
Dermoid cyst	1
Carcinomatous	1
Miscellaneous	
Salpingitis	33*
Adhesions	48*
Endometrial transplants	25†
*97.6 per cent. †30 per cent.	

corpus luteum was noted. Likewise, hyperplasia of the endometrium and fibroids of the uterus were noted in every case. Again, salpingitis and chronic inflammatory adhesions were found in 97.6 per cent of the patients while endometrial transplants were observed in 25 cases (30 per cent). While the 97.6 per cent of pelvic inflammatory disease offers a possible explanation for the follicle cyst formation and the subsequent ovarian dysfunction because of the disturbed blood supply to this organ, the high percentage of endometriosis again suggests a possible etiological source from hyperplasia of the endometrium.

III. The findings in a third group of 41 cases of fibroids and hyperplasia of the endometrium, although the evidence is indirect since the ovaries were not available for study microscopically, but were only commented upon grossly at the time of operation, likewise support the hypothesis of a cause and effect relationship between hyperplasia of the endometrium, ovarian follicle cysts, and fibromyomata. However, as noted previously, if follicle cyst formation, resulting in hyperestrin stimulation, is accepted as the cause of hyperplasia of the endometrium, the logical inference should follow that the findings of characteristic hyperplasia microscopically warrants the diagnosis of ovarian follicle cysts. Hysterectomy was performed in every case for multiple fibroids (Table III).

Hyperplasia of the endometrium was found in every instance. Likewise the operator commented upon the small ovarian cysts in each case. The operative observation of salpingitis

TABLE III

	Cases
Condition of myometrium	
Fibroids	41
Hyperplastic	6
Fibrotic	10
Adenomyomatous	1
Sclerotic vessels	3
Metritic	4
Endometrial transplants	3
Normal	18
Condition of endometrium	
Hyperplasis	41
Operative comment on ovaries	
Follicle cysts	41
Corpus luteum	0
Salpingitis and adhesions	40*
*97.5 per cent.	

Fig. 1. Typical macroscopic hyperplasia of the endometrium.

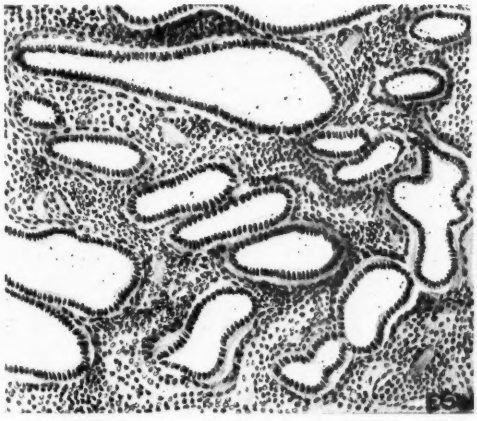

Fig. 2. Typical microscopic hyperplasia of the endometrium.

and adhesions was made in 40 cases (97.5 per cent), again a very high figure.

DEDUCTIONS

The evidence advanced by Schroeder, Meyer, Graves, Novak, and Fluhmann is certainly sufficient to warrant the acceptance of a cause and effect relationship between hyperestrin stimulation of the ovary and hyperplasia of the endometrium. Since the ovary reacts upon the uterus in its entirety, and not just upon the endometrium, some change in the myometrium should manifest itself from the unopposed action of estrin. One hundred and fifty cases of fibroids, associated with ovarian follicle cyst formation, and necessarily hyperestrinism, are offered to suggest a resulting fibromyomatous change in the myometrium, if the stimulation is prolonged sufficiently. If this be true, that hyperestrinism is the ignition, so to speak, of the fibromyoma, it does not follow that the hormonal stimulation has to persist after the growth is once present, as proved frequently in our clinical experience in observing the combination of myomata and pregnancy. In such a condition we know the morphology of the endometrium is decidua, and not the hyperplastic "Swiss cheese pattern." Whether the ovary is primarily responsible for the hyperestrin production or not is an unsettled question, but in view of the newer knowledge of the motor hormone control by the anterior hypophysis, it would seem more probable that the latter plays the important rôle, especially, since according to Novak, the administration of its hormone can produce beneficial clinical results in functional uterine bleeding. Moreover, it is contrary to the law of nature which maintains an external control over all organs or organisms that pass through a definite cyclic rhythm, that such an important organ as the ovary should maintain an intrinsic and automatic control over itself in having a beginning, continuance, and ending, as shown by woman in her functional years. Yet it does not follow that if the ovarian function or rhythm is disturbed that the anterior hypophysis is always the cause. Any structure involved in the mechanism of its function might be at fault, especially the blood supply, as evidenced by the frequency of cystic degeneration of the ovary from disturbed nutrition after hysterectomy or salpingectomy.

Moench is of the opinion that the follicle cyst formation of the ovary is due to ovarian congestion and increased blood supply to these parts, causing an increased number of follicles to ripen, and not to an inflammatory process as formerly believed. This observer explains the presence of functional bleeding around the menopause as due to increased

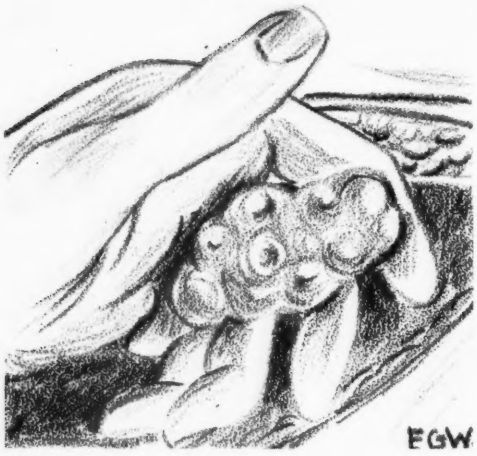

Fig. 3. Multiple follicle cysts of the ovary.

pelvic congestion, since women are heavier, less active, more constipated, and have, perhaps, lessened muscular tone. Favoring such an hypothesis Polak and Mazzola, in experimental torsion of the vessels around the uterus, parametrium, and contiguous tissues, found marked hyperplasia and hypertrophy of all uterine layers. In addition, there was a marked increase in the size and number of the blood vessels; also the connective tissue ratio of the entire organ was greatly increased.

In accepting ovarian and uterine congestion as a cause of follicle cyst formation of the ovaries and myomatous growths of the myometrium, many findings are left unexplained, particularly the high incidence of fibroids in the negro race, the absence of fibroids during pregnancy when the uterus is most vascular, and the non-development of fibroids in acute pelvic diseases and puerperal sepsis, when the vascularity of the uterus and adjacent structures is highly increased.

I am inclined to believe that the cause of formation of follicle cysts of the ovary is not to be found in a passive congested state of these organs and adjacent tissues, but as previously discussed, in the disturbance of the blood supply to these parts. The most frequent occurrence of this follicle cystic change in the ovary is at the two extremes of woman's reproductive life: at puberty the ovaries and uterus undergo development in size and function with a natural increase in the blood supply. If this supply cannot keep pace, as it were, with the anatomical and functional demands made upon it, naturally the organs must suffer from the insufficient blood supply, and the results are possibly manifested in the ovaries by follicle cystic changes. At the other extreme, the menopause, the reverse process occurs. The ovary has been passing through rhythmic monthly cycles, requiring variations of the blood supply to it, and supplying the demands made upon it by the organism as a whole; as the menopause approaches the ovarian blood supply is curtailed, as is seen in all other pelvic organs. If the blood supply becomes disturbed too quickly, might not follicle cystic formation result before the natural senile inactivity of the ovary takes place?

The ovaries of negro women are being studied in an attempt to show that disturbed ovarian blood supply, resulting from the high incidence of chronic pelvic inflammatory disease in this race, is the source of follicle cystic changes in the ovaries; the findings will be presented in another communication. For the present I need only quote Miller, who in 150 cases of fibroids in negroes, found tubo-ovarian disease in 93 per cent of the cases, and cystic degeneration of the ovaries in 80 per cent, while Alsobrook, in 100 cases of fibroids in negroes, noted salpingitis in 99.1 per cent. In the present survey both chronic infections and adhesions were observed in over 95 per cent of the cases in addition to the follicle cyst formation, and the ovarian stroma was considered atrophic, degenerative, and fibrotic in an equally high percentage.

If, as suggested by this paper, there be a cause and effect relationship between ovarian follicle cyst formation, resulting in immediate endometrial hyperplasia, and later in fibromyomatous growths of the myometrium, the work of Novak and Hurd offers great therapeutic encouragement as a prophylaxis against fibroid formation. These observers have obtained cessation of bleeding in 44 of 51 cases of functional uterine hæmorrhage by the administration of the anterior pituitary hormone and the restoration of the normal

menstrual rhythm seems apparent. If further study proves the result to be permanent, it would seem legitimate to predict a decrease in the incidence of fibromyomatous growths in the white race through the prophylactic treatment of ovarian hyperestrinism with the luteinizing factor of the anterior hypophysis.

SUMMARY

1. The various theories pertaining to the histogenesis and etiology of fibromyomata of the uterus are discussed.

2. Evidence is offered to show that the unopposed action of estrin, in the absence of the corpus luteum influence, is the cause of hyperplasia of the endometrium.

3. An hypothesis is advanced to suggest that the unopposed action of estrin on the myometrium, if prolonged sufficiently, would result in fibromyomatous growths.

4. Twenty-six cases of hyperplasia of the endometrium, in which operation was done and diagnosis as such made from microscopic study, and in which a second operation was performed for fibromyomata after an approximate interval of 4 years and 4 months, are analyzed.

5. One hundred and twenty-four cases of fibromyomata, diagnosed microscopically, are offered with their associated ovarian and endometrial findings, as presenting added evidence in support of a cause and effect relationship between ovarian follicle cystic formation, hyperplasia of the endometrium, and fibromyomata of the uterus.

6. An hypothetical conclusion is advanced that the unopposed action of estrin on the uterus results: (1) in immediate endometrial changes, characterized by hyperplasia, and (2) in more latent myometrial pathology in the nature of fibromyomatous growths.

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CLINICAL SURGERY

FROM DEPARTMENTS OF ANATOMY AND SURGERY, UNIVERSITY OF NEBRASKA

REPAIR OF HIGH LACERATIONS OF THE RECTUM WITH COMPLETE INCONTINENCE

ANATOMICAL PRINCIPLES AND OPERATIVE TECHNIQUE

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IT is interesting to note the accomplishments and successes that follow the varied techniques in the treatment of lesions amenable to surgical therapeusis. In most instances the principles are the same, the variation being in some of the details. I believe that when there is a choice, the simpler technique should be elected, provided reasoning and experience have proved that the more complicated procedure is unnecessary.

In a review of the literature on the technique used in repair of high lacerations of the rectum with complete incontinence, associated with third degree lacerations of the pelvic floor, the methods of fourteen different operators were consulted. Eleven of these, including Orr, Ristine, Noble, Tait, Ward, Emmet, Marcy, Goldspohn, Farrar, Kelly, and Crossen, used silver wire, silkworm-gut, or kangaroo retention sutures; only three operators, Titus, Watkins, and Clark, repaired the perineum and sphincter ani without the use of retention sutures. Despite the variance in this one principle of the technique, all of these authors claim equally good results. The first group, who employ retention sutures, usually of an unabsorbable nature, incur the disadvantage of the necessary removal of the sutures some days later. Also retention sutures cause more discomfort to the patient.

During the last 3 years I have performed the operation six times by the simpler technique of avoiding retention sutures and all have been successful, including one operation which was carried out 12 years after the primary injury. Although very few authors report this operation without the use of retention sutures, I believe if the principles for attempting an anatomical restoration are followed, with close adherence to careful operative technique and postoperative care, success is assured without the use of painful unabsorbable retention sutures which require removal.

The anatomy of the pelvic floor and its relation to the rectum and vagina have been well taught by Tandler, Halban, Edouard Martin, Testut, and Jacob (Figs. 1 and 2). The principles of pelvic floor repair have been sponsored by Emmet, Tait, Marcy, Watkins, and Ward. The principles and methods of repair for high lacerations of the rectum were first introduced by J. Collins Warren, in 1875. Ristine popularized this operation. Kelly initiated the individual suture of the sphincter ani muscle. Of late, Farrar has emphasized the use of this operation in extreme high lacerations of the rectum by dissection of the flap high on the posterior wall of the vagina just below the cervix.

The technique that is used in the repair of my cases is of the simpler type, in that no retention sutures are used. Over a period of 3 days prior to the operation, the vagina and rectum are well prepared by twice daily irrigations of 1:5000 potassium permanganate. On the day previous to operation the patient is on a liquid diet and on the evening before operation is given a normal saline enema, repeated until it returns clear. When the patient is brought to the operating room, both the rectum and vagina are thoroughly irrigated with a quart of 1 per cent lysol solution. During this stage of the operation I prefer to wear two pairs of rubber gloves so that if it becomes necessary the index finger of the left hand may be inserted into the rectum to act as a guide. The flap is outlined as indicated in Figure 3, and if the tear reaches quite high on the rectal wall there should be no hesitation in extending it up to the level of the cervix. As indicated in the small diagram, care must be taken that the distance from *a* to *b* is slightly greater than from *b* to *c*; otherwise, the flap will be of insufficient length, and it is the vaginal surface of this flap which, when turned down, becomes the anterior surface of the lower rectum and anus. Care must also be

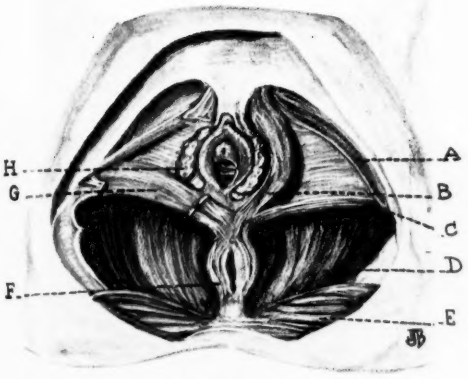

Fig. 1. Pelvic outlet exposed, with removal of the skin, labia, subcutaneous fascia, superficial perineal fascia, and contents of ischiorectal fossæ. *A*, Ischiocavernosus; *B*, bulbocavernosus; *C*, superficial transverse perinei; *D*, levator ani; *E*, gluteus maximus; *F*, sphincter ani; *G*, urogenital diaphragm; *H*, Bartholin's gland. (The superficial stratum, *A*, *B*, and *C*, has been removed on the right side, thus exposing the middle stratum, urogenital diaphragm. The levator ani is considered the inner stratum.)

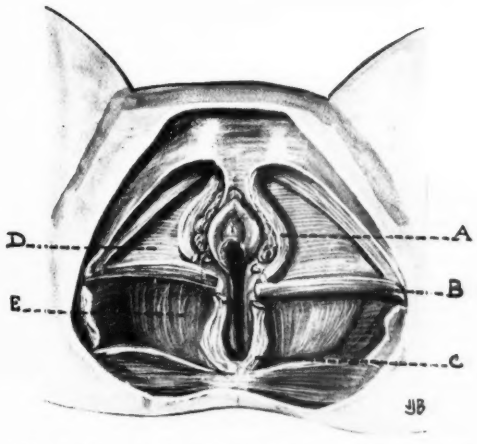

Fig. 2. There has been a complete laceration destroying the perineal body, with the resulting separation of the bulbocavernosus muscle, the transverse perinei muscles, the sphincter ani muscle, and the levator ani muscle. The vagina and rectum are now one cavity. *A*, Bulbocavernosus; *B*, transverse perinei; *C*, sphincter ani; *D*, urogenital diaphragm; *E*, levator ani.

exercised not to buttonhole the rectum. The flap in the anal margin must extend lateral to the dimpled or palpable ends of the sphincter ani muscle. When it has been turned down, as shown in Figure 4, the extra pair of gloves may be removed, and at this time the operative area and the rectum should again be irrigated with 1 per cent lysol solution. From now on, rectal contamination is not probable.

After this flap has been turned down by either blunt or sharp dissection, the levator ani muscles are found, particular care being taken to pick up these muscles far back from the introitus because the firmer and more accurate approximation that is made of the levator ani muscles and fascias around the rectum, the more they act as accessory muscles in sphincter control. Although simple interrupted sutures of No. 2 chromic catgut may be used, I prefer to use interrupted No. 2 chromic catgut figure-of-eight sutures to approximate the edges of the levator ani muscle. Usually about three sutures are necessary. This builds up a very good muscular wall separating the vagina and rectum and helps cover over the flap of vaginal mucous membrane which has been turned down to form the anterior wall of the rectum. As shown in Figure 5, several interrupted No. 1 chromic catgut sutures are then used to close the upper end of the vaginal exposed area by bringing together the edges of the mucous membrane and the margins of the urogenital diaphragm. This bringing together of the levator ani muscles holds the rectum somewhat forward and serves as a splint to the perineum for the repair of the sphincter muscle and the transverse perineal muscles. Both the superficial and deep transverse perineal muscles have been lacerated in the complete tear and approximation of these further strengthens the former central point of the perineum. Sometimes there is considerable difficulty in locating the ends of the transverse perineal muscles. These muscles just mentioned are usually sutured with No. 1 chromic catgut figure-of-eight sutures, both ends being brought to the central point anterior to the rectum. Careful search is then made for the ends of the sphincter ani. When the ends have been located, care must be taken not to isolate them too freely or more retraction is likely to take place and with fascia removed the sutures to be placed have less likelihood of holding. This surrounding scarred and fibrous tissue tends to splint the muscle and hold it in fairly good position. The ends are brought together by a No. 0 chromic catgut figure-of-eight suture and this suture in turn picks up a bite of muscular and fascial tissue in the newly made central point of the perineum (Fig. 6). An interrupted No. 1 chromic catgut suture closes Colles' fascia and brings the skin margins together

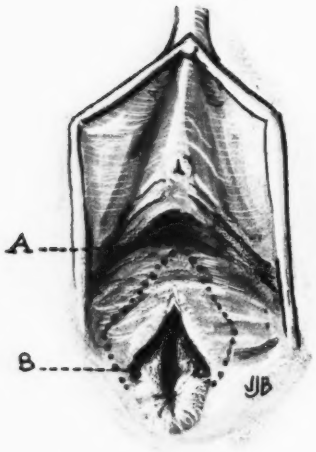

Fig. 3.

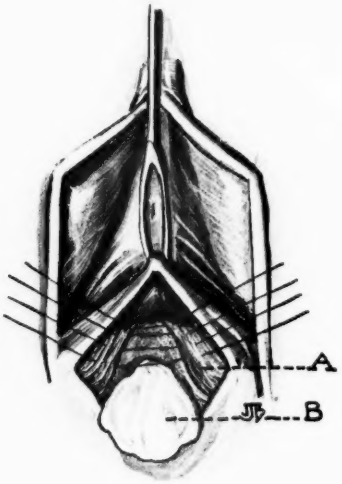

Fig. 4.

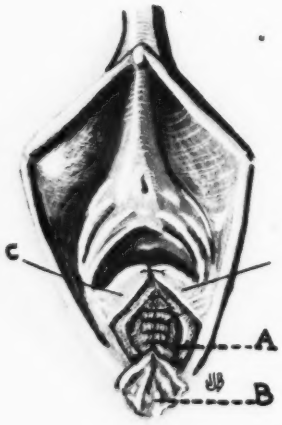

Fig. 5.

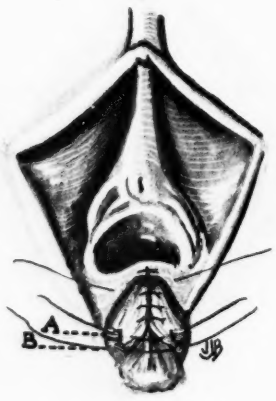

Fig. 6.

Fig. 7.

Fig. 3. Large cut: Outline of incision to be made into the mucous membrane of the vagina. Dissection is carried downward from point *A*. The margin of this flap must be outside of points *B* which usually indicate by small depressions or by palpation the ends of the lacerated sphincter ani muscles. Small cut: The length of the flap from *a* to *b*, which is the top of the laceration, must be as great or greater than, the distance from *b* to *c*. The mucosa of this flap when turned down faces the rectum and anus. Points *d* must be outside of the sphincter ends, *sp*.

Fig. 4. The flap *B* has been turned down and *A*, the levator ani muscles, exposed. Interrupted No. 2 chromic catgut sutures have been placed. This bridges over with muscle and fascia the defect present between the ...us and rectum.

Fig. 5. The levator ani sutures have been t...d. One suture in the mucosa has been tied and one is in p...e. The suture marked *C* is interrupted chromic catgut ...d must grasp the mucous membrane, and the torn edge ...he urogenital diaphragm.

Fig. 6. *A*, Suture grasping the transverse pe...ei muscles; *B*, suture grasping the ends of the sph...ter ani muscle.

Fig. 7. The mucosa and fascia have been c...ed with interrupted chromic sutures. *A*, Final pucke...r suture through flap and skin edges.

subcutaneously. A small purse string suture of No. 0 chromic catgut takes up the excess tissue of the flap and slightly puckers it around the anterior margin of the anus (Fig. 7). The operation is then completed by injecting 1 to 2 ounces of sterile vaseline into the rectum. This tends to act as a mold and as a protective dressing for the lower rectum and anus. However, its principal function is to serve as an effective lubricant at the time of the first bowel evacuation after operation.

The after-care of these patients is most important. The perineum must be kept clean by repeated external douches of 1:5000 potassium permanganate solution after each urination or bowel movement; in any event the douches should be given twice a day. The thighs must be kept together. The patient should be on a liquid diet without milk for 5 days and then on a soft diet for 5 days. Bowel evacuation is stimulated on the fifth day by giving citrate of magnesia. At no time are enemas given and after the fifth day constipation is prevented by giving petrolagar twice daily and a small dose of citrate of magnesia every other day if necessary. About the tenth day, rectal examination is made, at first introducing only the little finger. This should be repeated every 2 or 3 days in order to prevent any stricture formation.

Fig. 8, left. Rectum and vagina may be seen having one common external opening. No perineal body present. Photograph of Case 3.

Fig. 9. Same patient 2 weeks after operation, showing a strong perineal body with considerable tissue between the anus and vagina.

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ARRHENOBLASTOMA OF THE OVARY[1]

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WE are indebted to Meyer for calling our attention to the rather novel conception that tumors have function, much as any normal organ. This fact is ordinarily overlooked, although the cachexia associated with malignant disease has been noted for centuries. The best example of neoplastic function occurs in the ovary, which is the site of certain unusual tumors, notably the granulosa cell carcinomata whose secretions produce an exaggerated femininity as evidenced by precocity of sexual development in the young subject and rejuvenation in the old; and some of the arrhenoblastomata whose hormones not only defeminize, but masculinize their hosts. The term "arrhenoblastoma" (meaning to make like a male) as proposed by Meyer to cover this interesting group of masculinizing tumors of the ovary, numbering 26 in the literature today, is restricted to those tumors which show male characteristics histologically as well as clinically, and furthermore excludes those cases of ovariotestis or true hermaphroditism.

This case is being reported not only as an example of this extremely rare condition, but in order to illustrate the powerful influence exerted by sex hormones, both normal and abnormal, upon the development of the secondary sexual characteristics of the body.

REPORT OF CASE

One of us (J. M. T.) was called to see Miss M. E., Case No. 132-32, a white school girl, 18 years old, who entered St. Edward's Mercy Hospital January 30, 1932, complaining of severe abdominal pain, cough, fever, and pain in the chest. The family history was irrelevant except that both parents were born in Germany.

The past history was negative except for the extremely interesting story concerning the generative system. She began menstruating at the age of 13 years, with a regular interval of 28 days, moderate flow, without pain, lasting 4 to 6 days. At the age of 14 years the menstrual periods suddenly ceased and patient has not menstruated since that time. At the age of 16 years she noticed the development of excessive hair on the face and over the body, which was progressive to the extent that it was necessary to shave the face with increasing frequency. A change was also noted at this time in the voice, it at first becoming coarse, then developing a contralto quality and reaching the present stage of a very definite baritone.

The onset of the present illness occurred about 1 month previously when she noted pain in the lower part of the abdomen with progressive enlargement. A few days before admission she developed a cough, followed by pain in the chest, fever and the expectoration of blood tinged sputum.

Physical examination at the time of admission showed a very sick young white girl who was mentally alert, clear, and co-operative. The appearance of the face, with bushy eye-brows and marked beard, was very striking, and suggested that of a young man. The hair of the head, while short, was rather profuse. The temperature was 104 degrees orally, the pulse rate 158, and the respiratory rate 58. The blood pressure was 105/60. There seemed to be an excessive pallor to the skin and mucous membranes. The patient was coughing incessantly and at times expectorating blood tinged sputum. Dullness, approaching flatness, with suppressed breath sounds, was found over the entire posterior aspect of the left lung, with numerous coarse râles over the upper portion. The right lung was clear. The breasts were flat and atrophic. The nipples were coarse, pigmented, and a circle of long hair was present in the areola. No abnormalities were noted about the heart. There was a marked generalized hypertrichosis, especially noticeable in the axillæ, forearms, inside the thighs and around the perineum. The distribution of the pubic hair was of the masculine type with a heavy ridge in the midline extending up to and around the umbilicus. The abdomen was enlarged in the lower half due to an abdominal tumor the size of a 6 months' uterine pregnancy, and extending down into the pelvis. Tenderness in the left lower quadrant was so exquisite that the patient could hardly bear the weight of the bed covers on her abdomen. On vaginal examination the clitoris was found to be hypertrophied to three times normal size, with well developed prepuce, the hymen absent, and the vaginal canal contracted so as to admit one finger with difficulty. The cervix was small, soft, and the uterus could not be outlined. Motion was not communicated to the cervix by moving the tumor from above the symphysis. The mass could be felt partially distending the cul-de-sac and lateral fornices.

A markedly flat masculine type of pelvis with masculine type of skeleton was shown by the following measurements of pelvis and shoulders: Pelvis—spines 23.5 centimeters, crests 24 centimeters; trochanters 26 centimeters, external conjugate 15 centimeters, and ischiadic tuberosities 8 centimeters; shoulders—36 centimeters.

Clinical laboratory studies gave the following results: Blood examination showed erythrocytes 3,[illegible]20,000; hæmoglobin 60 per cent; leucocytes 17,000; differential—Schilling count—: juvenile cells, 2; staff cells, 17; segmented cells, 68; lymphocytes, 16; eosinophiles 0. Shift to the left 20; nuclear index 3½; malaria negative; Wassermann negative.

Urinalysis, 1.018; acid; trace albumin; no sugar; few unclumped white cells.

X-ray report by Doctor W. R. Brooksher, Jr.; abdomen, large dense abdominal and pelvic tumor; head, normal sella turcica; chest, massive pleural effusion, left side.

Patient continued to vomit frequently, and the abdominal pain persisted. Temperature remained elevated to 100 degrees, with the rapid respiratory rate persisting. On February 14, 1932, 2,800 cubic centimeters of dark bile colored fluid were aspirated from the left pleural space, following which there was considerable improvement in her general condition. This fluid was negative on culture and negative for tuberculosis by 6 weeks' guinea pig inoculation and autopsy.

The pleural fluid continued to reform and thoracentesis was performed 7 times, 1800 to 2500 cubic centimeters of fluid being removed at each sitting. The abdomen con-

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Fig. 1. Appearance of face with well developed beard and moustache. Note bushy eyebrows.

Fig. 2. Full view of body showing hypertrichosis, masculine pubis, and male type of skeleton.

tinued to be exquisitely tender, and in spite of the fact that patient was retaining some nourishment, she continued to lose ground. Operation had been deferred because of the pleural effusion and poor physical condition, but by April 14, 1932, the tumor had enlarged to the size of a full term pregnancy, and pressure symptoms were of such severity that surgical intervention was deemed imperative.

A pre-operative diagnosis was made as follows: (1) teratoma of the ovary with a preponderance of functioning testicular tissue. (2) the possibility of true hermaphroditism, with destruction of the ovarian tissue by neoplasm, probably malignant, and functioning of the testicular tissue, was also considered.

On April 14, 1932, under spinal anæsthesia, administered by Dr. M. E. Foster, laparotomy was performed by two of us. (Drs. J. M. T. and S. J. W.)

Operation. A low midline incision was made, and when the peritoneal cavity was opened approximately 3,000 cubic centimeters of thin brownish fluid escaped. The tumor was found to be semicystic, and of the size of a full term pregnancy, extending from the pelvis to the xiphoid process of the sternum. Since it could not be delivered through the incision, which was extended 4 centimeters above the umbilicus, the volume was somewhat reduced by aspirating 4,000 cubic centimeters of thin brown fluid from several cysts. Adhesions to the liver and viscera of the upper portion of the abdomen were broken up and the tumor was delivered. It was then found to be an intraligamentary tumor arising from the region of the left ovary, and was removed by dissection from the leaves of the broad ligament and ligation of the pedicle. Raw areas were well peritonized. The right ovary was smooth, brown, half the usual size, and did not show the slightest evidence of formation of graaffian follicles or corpora lutea. Both tubes were normal. The uterus was one-third the usual size, and apparently otherwise normal. The wound was closed in layers without drainage and the patient returned to her room in good condition.

The convalescence was extremely smooth, and it was a notable fact that there was no further recurrence of the pleural effusion. X-ray examination failed to demonstrate chest metastases. The appetite and strength rapidly returned and she was discharged from the hospital greatly improved in good condition May 10, 1932.

A decided change in the appearance of the patient was soon noted. Menstruation occurred for the first time in 4 years on May 22, 1932. It has occurred regularly at 4 week intervals and 3 to 5 days' duration since this time. A normal feminine type of voice was noted July 24, 1932. At the present time, September 30, 1932, the patient has gained 40 pounds in weight, a marked hypertrophy of the breasts has taken place and the normal feminine habitus has been resumed. The clitoris and prepuce are less prominent. An abnormal growth of hair is still apparent over the chin, but it is of a much finer texture and of lighter color. The patient now shaves once in 5 weeks instead of every 3 to 4 days, as formerly.

Gross pathology. A great portion of the weight and volume of the tumor had been lost due to evacuation of multiple cysts. After removal the tumor measured 20 by 20 by 18 centimeters. The weight was 900 grams. The tumor grossly resembled the ordinary multilocular serous cystadenoma. There was a well developed fibrous capsule which had not been broken through and was smooth for the most part except at the uppermost portion which had been adherent to the liver. Large tortuous blood vessels were visible through the capsule. The pedicle was broad and vascular. On section some of the cysts were found to contain masses of soft greyish, friable material. The solid portion of the tumor had the consistency of a normal ovary, although ovarian tissue as such could not be recognized. Unruptured cysts contained thin brown fluid.

Microscopic pathology. Sections were cut from many different portions of the tumor and show two distinct types of morphology, each of which is undergoing degeneration on one hand and active proliferation on the other. The bulk of the tumor is made up of an atypical arrangement of small round and spindle cells, showing an occasional whorl and a suggestion of groups being bound together in fasciculi. The majority of the nuclei are oval to round, irregular in size, and for the most part hyperchromatic. Mitotic figures are common. A few of the nuclei are pale, large and filled with dark granules. In the more cellular portions of the tumor there is no evidence of stroma. A rich network of thin walled, poorly constructed capillaries is generally present.

Some areas of the tumor show a well marked coagulation necrosis and infiltration by small lymphocytes. Other areas give evidence of hæmorrhage, and in some fields hyaline degeneration. Where a stroma is present, it consists of an œdematous, fibrillated, white connective tissue.

The cyst walls consist of loosely arranged white fibrous connective tissue, rather deficient in nuclei, very vascular, and in some areas invaded by an entirely different type of cell which is epithelioid, filled with lipoid, and can be identified as an interstitial cell. Figure 8 depicts these cells. There is no epithelial lining to the cysts. It may be conjectured that they have arisen as the end-result of coagulation and liquefaction necrosis of portions of the tumor.

Other blocks show the structure to be undoubtedly epithelial as illustrated in Figure 7. This tissue came presumably from the region of the hilum of the ovary and

Fig. 3. Contracture of vagina and hypertrophy of clitoris. Prepuce well developed.

represents the primary growth. The cells are arranged in the form of irregular medullary cords (Fig. 7) and also as rudimentary tubules (Figs. 5 and 6). As shown the tubules are lined with a single layer of atypical columnar to cuboidal epithelium without basement membrane. Cellular detritus and coagulated material have collected in some of the lumens, and in a few, definite pear-shaped forms, suggesting atypical spermatozoa, can be made out. Such an instance is clearly shown in the lower right hand corner of Figure 6.

And of especial significance is the resemblance of many of the intervening cells, as pointed out by Novak, to a condensed and hyperplastic rete ovarii structure.

It is therefore our contention that this tumor is primarily an epithelial tumor, originating in the hilum of the ovary, and developing from anlagen in the rete consisting of residual undifferentiated cells which have developed along male lines as evidenced by the presence of tubules similar to seminiferous tubules and of typical testicular interstitial cells. This histological evidence is the link of proof needed to stamp this tumor as an arrhenoblastoma primarily, which has undergone secondary sarcomatous degeneration.

INCIDENCE

There are no reliable figures on record as to the incidence of this rare tumor. At the present writing, of the 26 reported cases none has occurred in the United States. Other cases have occurred, as an undoubted case of Casler's, but have not been reported. Since Meyer's illuminating work, additional cases will undoubtedly be added with increasing frequency. The tumor occurs chiefly between the age limits of 21 and 35 years.

SYMPTOMS

1. *Defeminization.* The earliest sign has usually been a persistent amenorrhœa with sterility. There is a tendency for the hair of the head to fall out and be short. The breasts atrophy and abnormal deposits of fat may occur over the body. The genitalia of the individual are hypoplastic with the exception of the clitoris. The vaginal canal is short and contracted, the body of the uterus and cervix atrophic or infantile, and the opposite ovary small and entirely free from graaffian follicles. The libido has been unchanged until late in the disease.

Fig. 4. Gross appearance of tumor.

2. *Masculinization.* The skin is usually dark, rough, and shows a tendency to an acne eruption. There is an abnormal and excessive development of hair over the body. A beard, necessitating in some cases daily shaving, is usually present. The distribution of hair over the pubis is of the masculine type. Hair may be present around the nipples. The facial expression is masculine, due to the coarse features and bushy eyebrows. There is an enlargement of the larynx, resulting in a lowering of the pitch of the voice. The skeleton is heavy and there is an inversion of the normal "pelvis to shoulders ratio" of the female. The musculature is correspondingly affected. The clitoris is hypertrophied in most long standing cases.

3. *Pain.* This symptom is usually present because of the pressure produced by a rapidly growing pelvic tumor. This pain may be constant or aggravated by micturition or defecation.

4. *Blood changes.* Secondary anæmia is usually present and an increase in eosinophiles and monocytes has been noted. The temperature is frequently elevated. The Aschheim-Zondek test is negative.

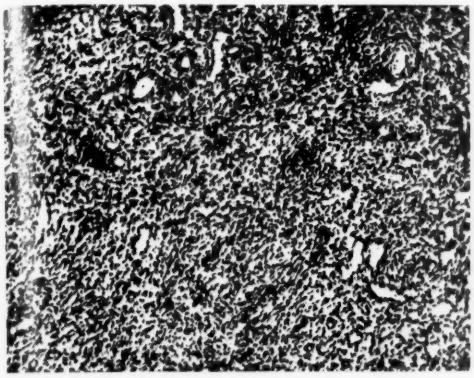

Fig. 5. Photomicrograph showing the tubules as they appeared under low power magnification.

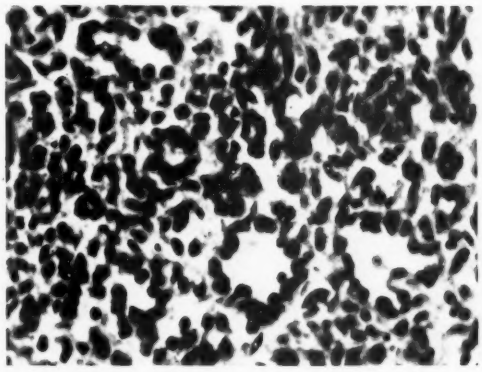

Fig. 6. High power magnification showing structure of tubules. Note pear shaped form in the lumen of one tubule.

5. A restoration of the normal female characteristics occurs after removal of the tumor with remasculinization upon recurrence. Normal pregnancy has occurred after operation in a number of the reported cases.

DIAGNOSIS

The association of a growing pelvic tumor with amenorrhœa naturally suggests pregnancy, which has been the usual tentative diagnosis made in these cases. The coarsening of the features indicative of beginning masculinization also may be interpreted as the normal accompaniment of pregnancy. However, the Aschheim-Zondek test will absolutely differentiate the two. The development and development of outspoken masculine characteristics, in an individual previously normal, under the above conditions should certainly suggest this tumor clinically. The finding of evidence of rudimentary testicular cells in the tumor microscopically confirms the diagnosis.

TREATMENT

The treatment is extirpation of the tumor, without disturbing the remaining pelvic organs, since one ovary is all that is affected and retention of the secretion of the other is essential to effect return to the normal feminine state. With the present state of our knowledge, and for the same reason as above, prophylactic deep X-ray therapy

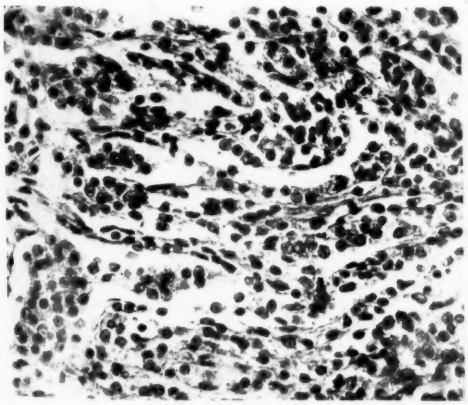

Fig. 7. High power photomicrograph showing the irregular epithelial cord-like structure. (Courtesy of Dr. Robert Meyer.)

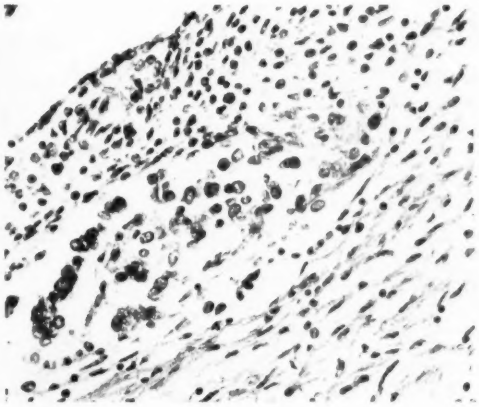

Fig. 8. Lipoid-containing epithelial cells found in periphery and in stroma of tumor. These are interstitial cells. (Courtesy of Dr. Robert Meyer.)

Fig. 9. Five months after operation. Note marked hypertrophy of breasts, return to feminine contour of hips and thighs, lessened hypertrichosis. Weight gain, 40 pounds. Compare with Figure 2.

does not seem to be indicated. In the event of recurrence, deep X-ray therapy should be of value because of the marked sensitivity of germinal epithelium to destruction by radiation.

PATHOLOGY

As a rule the arrhenoblastomata show marked cystic degeneration so that often solid portions may be very sparse. A number of cases of masculinizing tumors of the ovary previously reported as sarcomata or multilocular cystadenomata may fall into this classification after restudy. This is particularly true of the group in which the signs of masculinization have not been outspoken clinically. Histologically there appear to be three distinct groups according to Meyer:

1. *Adenoma testiculare.* Nine of the reported cases fall into this group. The structure is very similar to the tumor of the same name occurring in the testis, and is predominantly tubular. Masculinization clinically is the exception rather than the rule.

2. *Atypical group.* The 11 cases falling in this group showed marked masculinization in 9 instances. The case here reported is an additional instance. The structure is sarcoma-like and the tubules often rudimentary.

3. *Intermediate group.* In all 6 cases collected by Meyer, masculine changes of a slighter degree were present. Morphologically these tumors resemble group 1 in some areas and group 2 in others.

With the present state of our knowledge concerning sex differentiation, Meyer's theory of the origin of these tumors from undifferentiated germ cells in the hilum of the ovary, which have not been utilized during embryonic development of the ovary, but which have retained their sexual potency and remained dormant until some such time when for an undetermined reason proliferation takes place, is most compatible. Pick's theory that these tumors develop from an ovario-testis is not tenable in view of the fact that these patients do not exhibit evidence of bisexuality from birth, and that true hermaphrodites have never been known to develop tumors which defeminize and masculinize.

It is an interesting speculation why the most marked changes toward masculinity occur in the atypical group with sarcoma-like structure. These tumors in which the tubular arrangement is best developed are rarely associated with alterations in the secondary sexual characteristics of the individual, and in true seminomata, practically never. In the instance here reported, the sarcomatous appearance almost completely masks the tubular structure, although clinically extreme masculinization had occurred and return to femininity is in progress after extirpation of the tumor. Meyer is of the opinion that under certain conditions a transition is possible from epithelial to connective tissue. It has been assumed that the endocrine secretion of the testis, and presumably also the hormone affecting the secondary sexual characteristics of the body, is a product of the interstitial cells of Leydig, which exist under normal conditions in the form of irregular cords and which cannot be distinguished histologically as epithelial or mesodermal, although embryologically the bulk of the evidence is in favor of origin from the latter. It is the opinion of one of us (F.K.) that possibly an excessive amount of this hormone is produced by this hyperplasia of residual undifferentiated cells with definite male tendencies in the hilum of the ovary, or in other words a hyperplasia of anlagen of Leydig's cells, and that the tubular formation is merely another form of expression of tumor function and of the underlying tendency toward masculinity. Since normally interstitial cells cannot be classified exactly from the standpoint of tissue groups, it is tenable that under abnormal conditions this confusion should be even greater. Meyer has also suggested the possibility of a secondary sarcomatous degeneration of the stroma of the tumor.

In this particular case, recurrence will undoubtedly take place, since the removal was necessarily incomplete because of adhesions to the liver. Light may be shed upon this question by a study of the morphology of the recurrence. It must be emphasized, however, that while primary ovarian sarcomata are not uncommonly seen, masculinizing changes associated with such tumors only occur where epithelial elements

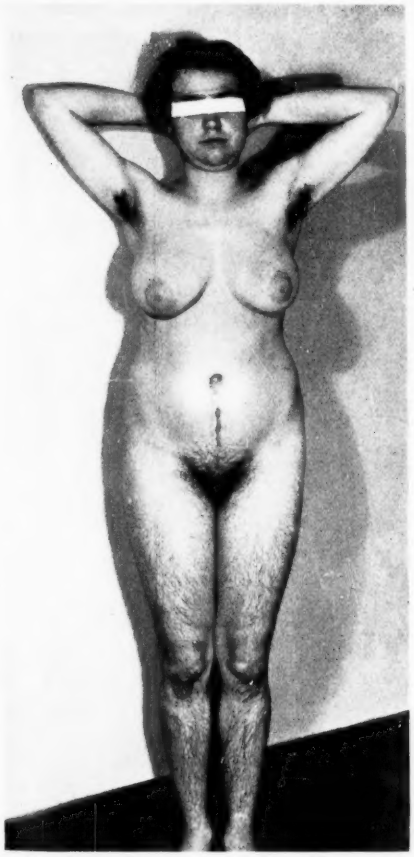

Fig. 10. Five months after operation. 40 pounds weight gain; return to general body type of feminine contour.

having the histological structure described by Meyer under the term arrhenoblastoma are present.

PROGNOSIS

These tumors are predominantly malignant. In the 8 cases reported up to 1909, only 1 was malignant. In 13 cases collected by Strassman since this time, all have been malignant except one. The case here reported shows malignant degeneration. This malignancy, however, is usually relatively benign, as recurrence and metastases do not usually make their appearance before 6 to 7 years.

SUMMARY

This case of arrhenoblastoma of the ovary is reported as the first case from the United States,

Fig. 11. Compare with Figure 1. Five months after operation. Lessened hair growth, of finer texture. This growth of beard of 5 weeks' duration; Figure 1 of 4 days.'

and the twenty-seventh in the literature in order to call attention to this condition which if generally appreciated and recognized would offer an exceedingly fertile field for increasing our knowledge of endocrinology by means of animal experimentation with tumor transplants, extracts, and transudates.

NOTE.—The authors wish to express their indebtedness to Dr. Emil Novak, of Baltimore, Md., for his valuable suggestions; to Dr. J. L. Goforth, of Dallas, Texas, for the histological sections which made this study possible, and for the preparation of part of the photomicrographs; and to Professor Robert Meyer, of Berlin, Germany, for his study of the tumor and photomicrographs.

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TREATMENT OF FRACTURES OF THE BONES OF THE LEG[1]

JAMES WILLIAM MARTIN, M.D., F.A.C.S., OMAHA, NEBRASKA

CURRENT surgical literature is so full of articles dealing with the use of skeletal traction in the treatment of fractures that any further contribution along this line might be promptly regarded as superfluous. The writer is emboldened to submit this paper dealing specifically with treatment of fractures of the bones of the leg because of the conviction that the technique to be described has both simplicity and dependability to recommend it.

Those who have had wide experience in treating fractures will readily agree that fractures of both bones of the leg often present an especially troublesome surgical problem. The fact that many of these fractures are compound adds, of course, to the difficulties. Whichever the type of fracture, that is, simple or compound, extensive injury to the soft parts and serious disturbance of the local circulation about the ends of the fractures, are frequent accompaniments. One need reflect but a moment upon the incidence of delayed or non-union in these fractures to agree with this statement. When the position of fragments approximates anatomical perfection, and there is no local infection or general constitutional factor to explain the failure of prompt union, there can be only one cause of delayed union, namely a disturbance in the local physiology induced by tissue and particularly minute blood vessel trauma. Any reduction procedure which adds more traumatism to the fracture site is physiologically wrong, and should be avoided.

Obviously the procedure which adds the greatest burden to the already embarrassed local physiology is open reduction and direct internal fixation with non-absorbable material. This does not mean that open reduction and fixation with metal will invariably be followed by failure; common experience disproves that this is a universal truth. But the implication is that this method will inevitably show a rather high percentage of poor results in terms of delayed or absolute non-union, inasmuch as it is inimical to the normal healing process.

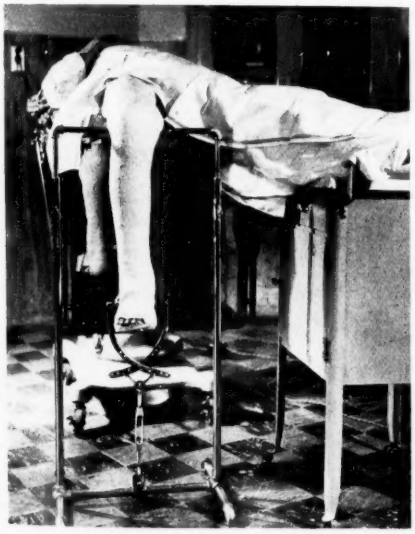

Fig. 1. After the skeletal traction device, either Steinmann or Kirschner type, is in place the knee is flexed over the upper cross bar of the frame and the traction bow is hooked onto the turnbuckle. (The frame is made of half-inch pipe except for the upper sliding unit which is one-quarter inch.)

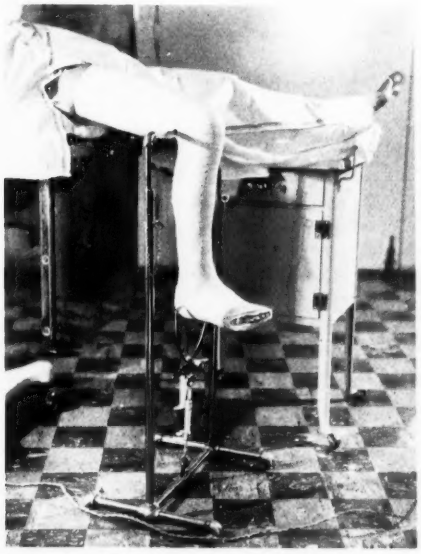

Fig. 2. The upper cross bar is pulled up as far as possible, depending upon the length of the particular leg, and it is held in place by inserting the keys (seen here attached to the small chain). It will be noted that there is ample room for application of the cast.

[1]From the Department of Orthopedic Surgery, Creighton University School of Medicine.

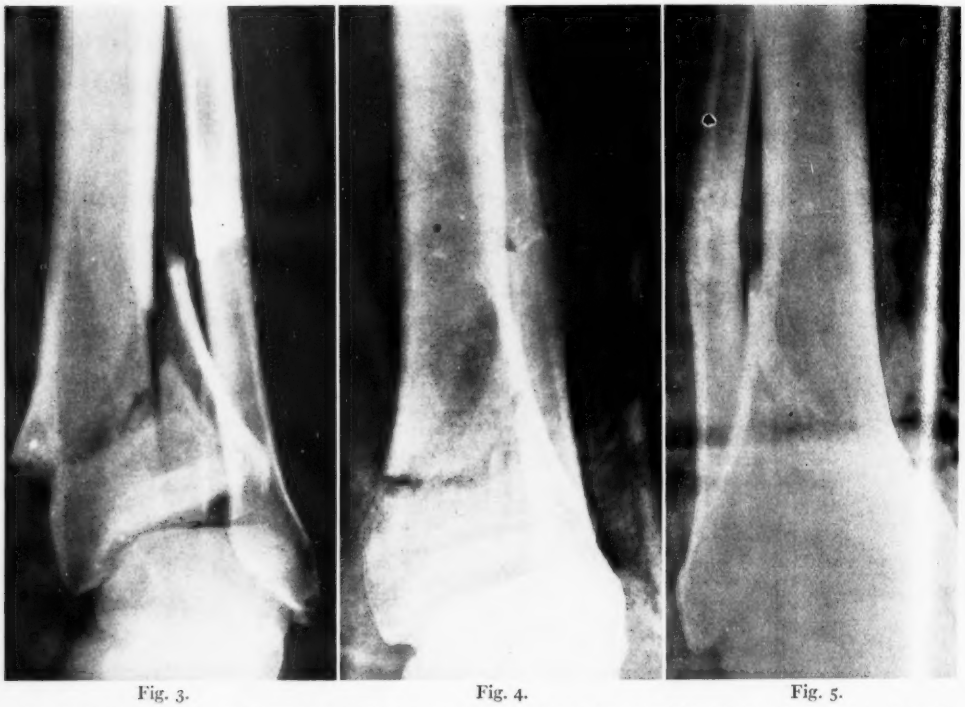

Fig. 3. Fig. 4. Fig. 5.

Fig. 3. Case 1. Compound comminuted T fracture of tibia extending into ankle joint, and simple transverse fracture of fibula. Patient a male aged 35 years.

Fig. 4. Case 1. Position after application of skeletal traction on frame and fixation in plaster. Note distraction or overpulling of tibial fracture.

Fig. 5. Case 1. Correction of overpulling and angulation by removal of section from cast.

There can be little justification for the internal metal fixation method in these leg fractures if it is quite uniformly possible to effect by means of the closed method an approximately anatomical reposition of fragments. It is the purpose of this paper to describe a technique of closed reduction in fractures of the bones of the leg which does insure this desideratum.

TECHNIQUE

This technique is simply the application of traction in an efficient completely controllable manner, followed by fixation in such a fashion that the correction or reduction of the displaced fragments is maintained with accuracy and permanency. Traction applied by the operator tugging with his unaided hands on the foot of the patient while an assistant vainly tries to exert countertraction on the knee, thigh, or crotch is not efficient traction because, though reduction may be momentarily obtained, it cannot be maintained during the application of the fixation apparatus whether cast or splint. Traction applied on a fracture table through adhesive tape and moleskin stuck on the skin of the leg is very frequently not efficient traction, particularly when fractures are situated low in the shafts. Traction to be efficient in these fractures must be skeletal traction. It must be employed in such a way that reduction will be obtained immediately, so that definitive fixation of the fragments may take place immediately. Nature does not wait 2 or 3 weeks or any other period before starting the work of healing. The "stimulus of incompleteness" exerts its influence at once. A skeletal traction technique which carries out gradual reduction by weight and pulley over a period of several hours or days is prone to too many accidents. It frequently does not give the operator the complete, accurate, mechanical control of the situation which he should have, and in addition it may be distressing to the patient.

Fig. 6.

Fig. 6. Case 2. Anteroposterior roentgenogram taken before reduction.

Fig. 7.

Fig. 7. Case 2. Anteroposterior view after reduction.

Fig. 8.

Fig. 8. Case 2. Lateral view after reduction.

The mechanical requirements of reduction and fixation are well met in the following technique:

1. A skeletal traction device, either Steinmann pin or Kirschner wire, is inserted through the calcaneus or just above it. Placing the pin or wire completely through the bone is preferable because it gives more certain control of the rotation of the distal fragments. (In some instances tongs inserted into the malleoli are preferable, e.g., when a fracture of the calcaneus is present in addition to the tibial and fibular fractures.) If the Steinmann pin is used, the unjointed pin and not the type that screws together in the middle should be selected. The latter breaks too readily.

2. The patient is next moved down on the table so that his buttocks are opposite the lower edge of the table, and his knee on the injured side is flexed to a right angle over the upper cross bar of the frame. The uninjured leg may be supported on another stand.

3. The Kirschner wire or Steinmann pin device is next attached to the turnbuckle fastened to the lower cross bar of the frame.

4. The adjustable upper cross bar of the frame is next pulled up as far as possible (depending upon the length of the leg) carrying the flexed knee with it; and the keys are inserted into the uprights to hold the cross bar in place.

5. Further traction is then obtained by twisting the turnbuckle until the fragments are pulled into place. Frequently reduction is perceived by the hand applied to the sides of the leg at the fracture level. A further check on length is had by comparing the measurements from the knee joint line to the tip of the internal malleolus on both legs in corresponding positions. And finally roentgenograms of the leg are made in the anteroposterior and lateral positions, a portable unit being wheeled into the operating room for this purpose.

6. While the films are being developed, application of a plaster cast is begun with the knee in right angle flexion and traction still maintained. Molded splints are used as the foundation for the cast and the cast is fashioned in sections above and below the line of fracture. (No plaster is wrapped around the upper cross bar of the frame in order that the leg may be eventually lifted off the frame without difficulty.) By the time the upper and lower segments of the cast are finished, the roentgenograms have been developed

Fig. 9A. Fig. 9B. Fig. 10. Fig. 11.

Fig. 9. Case 3. Anteroposterior and lateral views before reduction.

Fig. 10. Case 3. Anteroposterior view after reduction.
Fig. 11. Case 3. Lateral view after reduction.

and are available for examination. Any further correction of the position of fragments which is indicated is easily obtained; and the two segments of the cast are joined together with a few additional turns of the plaster bandage. The pin or wire is removed from the heel as soon as the cast has hardened unless the fracture is severely compounded, in which case there may later develop a further need for skeletal traction as will be mentioned later. The hiatus in the cast at the back of the knee found when the leg is lifted off the frame is filled in with a short molded plaster splint and a few circular turns of plaster bandage.

7. As soon as the cast is completed, it is slit or cut through its entire length, usually on its external lateral side, to lessen circulatory interference. This is a very important step and should never be omitted. The cast is prevented from becoming too loose by encircling it in three or four places with webbing straps or simple adhesive tape.

Reduction is, of course, performed under general inhalation or spinal anæsthesia. In my experience the latter is much better because it gives such complete muscle relaxation.

If the surgeon is so situated that immediate X-ray examination during the reduction procedure is not available, measurements and the gross appearance of the limb must be relied upon, and the cast completed at once. In this case the wire or pin is left in the heel; and check-up roentgenograms are made some hours later or on the following day. If these films reveal the need for further traction or correction of angulation deformity, the plaster cast, provided it has been carefully applied, affords the mechanism for complete correction. If the fragments are end to end but in faulty alinement the cast is cut through for about three-fourths of its circumference at the level of the angulation deformity; the angulation is easily corrected without anæsthesia and the corrected position is maintained by a few turns of plaster bandage re-inforcing the plaster cast. If further traction is needed the cast is cut through its entire circumference at the level of the fracture, traction is again applied to the heel pin sufficient to correct the shortening, and finally the proximal and distal portions of the cast are joined together with molded strips and a few turns of plaster bandage. Conversely, if the fragments have been over-

pulled a ring of plaster of the proper width is removed from the cast at the level of the fracture, and the two segments again fastened together with plaster.

POST REDUCTION TREATMENT

There is no need for haste in removing the pin from the heel, but similarly there is no point in leaving it in place after it has served its purpose. In simple fractures the pin is removed as soon as the check-up roentgenograms reveal no need for further traction. In compound fractures, the time for removal of the pin depends upon the absence or presence of frank infection in the fracture wound. If no infection has developed at the fracture site by the end of the first week it is concluded that there will be no further need for the pin, and it is removed; if during this period infection extensive enough to require removal of the cast has occurred the pin is left in place and utilized during subsequent treatment of the injured limb in a Thomas splint.

The thigh portion of the plaster cast is discarded about the end of the fourth week to permit mobilization of the knee, and at this time a walking-iron is fastened to the leg cast with a few turns of plaster bandage. The walking-iron should be applied with care or it will prove more of a hindrance than an advantage. The long axis of the iron should coincide with the long axis of the leg, and the iron should extend not more than 2 or 2.5 inches below the cast, it being assumed that the foot has been correctly placed at a right angle with the leg. The sole and heel of the shoe on the uninjured foot usually need to be elevated a little to equalize the length. Weight bearing is now freely permitted, first with crutches until the weakened quadriceps femoris muscle has regained some strength, and then with a cane. The cast is usually completely discarded about the tenth week in the severer fractures. The criterion, of course, is the roentgenological and clinical evidence of union. The period of total disability should not exceed 14 weeks in a patient employed at heavy common labor, provided there has been no infection or other complication.

SELECTION OF CASES

This technique of immediate reduction by means of skeletal traction on the specially constructed frame followed by immediate fixation in plaster is applicable to practically all fractures of the shafts of the tibia and fibula with considerable displacement whether simple or compound. In compound fractures débridement is sparingly performed, only the skin edges and the frankly devitalized muscle tissue being excised. The wound is packed with vaselinized gauze and no attempt is made to bring the skin edges together, though a few silkworm sutures are inserted chiefly to control oozing. Copious dressings are then laid over the wound and bandaged in place, after which the pin or wire is inserted into the heel just as in a simple closed fracture. No window is cut in the cast and the compound fracture wound is not dressed as long as the patient's temperature does not become alarming. If frank infection does develop it is, of course, treated according to common surgical principles.

ADVANTAGES OF THE TRACTION FRAME

The chief advantage of the traction frame over the standard fracture tables in the treatment of the fractures here under consideration is that it permits traction on the leg with the knee flexed to 90 degrees with a minimum of bother and a maximum of control. And there can be no difference of opinion regarding the preferable position of the knee during reduction of these fractures; the right angle flexion position is by far the better. It is better than the extended position because it gives additional relaxation to the calf group of muscles, because it affords a perfectly fixed point of countertraction, and because it renders redislocation of the reduced fragments after application of the cast impossible. I think this particular frame has perhaps some advantages over the apparatus used by Boehler inasmuch as angulation at the site of the fracture is less likely to occur with the leg in the dependent or vertical position than it is with the leg in the horizontal position; furthermore this frame interferes less with application of the plaster cast; and finally it is simpler to construct. Other advantages of the frame besides its efficiency are its inexpensiveness and portability. It may be used for fractures other than those of the tibia and fibula though this does not come within the scope of this paper.

SUMMARY

1. Open reduction and internal fixation by means of non-absorbable material in fractures of the bones of the leg is too frequently followed by delayed or non-union.

2. Closed reduction will give a high percentage of good results in terms of shortened convalescence and minimal functional impairment provided skeletal traction is properly employed.

3. A technique of closed reduction by skeletal traction, and details of post reduction treatment are given, and a simplified traction-frame is described.

COINCIDENT SURGICAL EXPOSURE AND RADIUM THERAPY IN THE TREATMENT OF EXTENSIVE CERVICAL CANCER[1]

ARTHUR H. CURTIS, M.D., F.A.C.S., CHICAGO

THE number of cures of cervical cancer varies roughly from 25 to 30 per cent in the major clinics of all countries, irrespective of whether the growth is removed or is treated by radium. Generally speaking, the results are very satisfactory in cancers not progressed beyond Stage I, in which cases the growth is still limited to the uterus.

In Stage II cancer of the cervix, in which the growth has progressed beyond the uterus but is still relatively limited in extent, the prognosis is dubious; in Stage III cases, with induration of the parametrium and more or less fixation of the uterus, the outlook is well-nigh hopeless. In brief, radical operation and radium treatment are relatively unsatisfactory both in Stage II and in Stage III cases, and it is apparent that other procedures are required for successful management of patients with these more extensive lesions. Radical operations have evidently reached their limit of efficiency and we therefore turn now to improved radiation and allied measures for further help.

In the pioneer days of radium treatment, attempts to obtain cures with massive doses resulted in a distressingly high incidence of destructive lesions of the adjacent viscera, often terminating in fistula formation or death. We learned relatively early that the pelvic viscera are highly susceptible to injury from radium burns and, particularly, that many cancers can not be cured because proximity of the bladder inhibits efficient radiation. With this in mind, I have for several years made a practice of separation and upward displacement of the bladder to permit more extensive use of radium in this region without introducing the danger of vesical fistula. The additional area thus made available for radiation has permitted intensive treatment of several cases of cervical cancer which could not otherwise have been satisfactorily radiated.

The value of dissection and retraction not only of the bladder but also of the other vulnerable tissues has become more and more apparent and has eventuated in a combined method of surgical exposure and coincident radium application. The suggestions advanced in this paper pertain particularly to treatment of the Stage II group of cases and to the less advanced cases of the Stage III group in which there is some hope of cure.

PROCEDURE

The necrotic cervical growth is treated with surgical diathermy or prophylactic radiation at least 3 weeks prior to operation. Preliminary deep X-ray therapy may serve equally well in healing the sloughing cancerous surface.

Under anæsthesia, a preliminary pelvic examination is made to determine the extent of the growth and the amount of intervention required. Exposure of the cancer-bearing uterus and adjacent cellular tissues is now undertaken. With blunt dissection, the bladder is mobilized upward, the cervix encircled with an incision as in making a radical vaginal hysterectomy, and the vaginal mucosa painstakingly dissected laterally and posteriorly, along natural lines of cleavage. The body of the uterus and the regions of the broad ligaments and cardinal ligaments are now well visualized. With the organ half delivered broadside, vaginally, the bladder safely anchored in its elevated position with a catgut suture holding it high on the uterus, and the paracervical tissues exposed, a massive radium treatment is possible. Radium needles or radon seeds are now inserted where needed, near to or into the cervix or far from it, as indicated, with assurance of safety of the adjacent vulnerable organs (Fig. 4). Although the ureters are subject to possible injury, they are considerably retracted incident to the dissection and displacement of the bladder and are relatively immune. Preliminary ureteral catheterization may merit consideration in selected cases, but we have not resorted to it. Injury of a uterine artery is a possibility; I have not yet seen that complication despite many years' custom of introducing radium needles into the cervical parametrium. Palpation of the artery preliminary to burying a radium needle in its vicinity appears unnecessary.

After burying the radium needles (or radon) as described, a chain tandem of radium capsules is inserted into the uterine canal in the usual manner. A vaginal pack completes the procedure.

Until further experience warrants, the total radiation should not exceed 3,500 milligram-hours. Even that amount may be excessive.

REPORT OF CASES

CASE 1. Patient was admitted to Passavant Memorial Hospital January 9, 1933. She was a married woman of 58

[1] From Passavant Memorial Hospital and the Department of Obstetrics and Gynecology, Northwestern University Medical School.

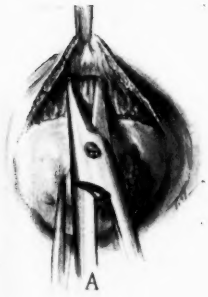

Fig. 1.

Fig. 2.

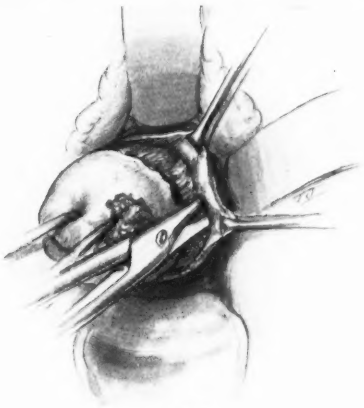

Fig. 3.

Fig. 1. The bladder is mobilized and displaced upward.
Fig. 2. The cervix has been encircled with an incision. Early stage of dissection of the vaginal mucosa.
Fig. 3. The vaginal mucosa is painstakingly dissected anterolaterally and posteriorly along natural lines of cleavage.

with two healthy children. Menopause occurred at 39 years of age; slight spotting of blood 19 years later, in September, 1932. Rather free bleeding on one or two occasions thereafter. No pain.

Examination. Patient's general condition was good; heart and lungs were normal, blood pressure 130/88; red blood count, 4,720,000; hæmoglobin, 75 per cent; Wassermann, negative. Vaginal examination revealed some urethrocele with incontinence, a relaxed perineum with slight rectocele and a long, narrow, funnel shaped vagina. The cervix, high up in the vaginal vault, nearly 4 inches from the vulva, presented a friable new-growth involving both lips. The cancerous tissue bled freely on manipulation. The wide extent of the growth in the cervix suggested some invasion of the parametrium. The uterus had limited mobility, but there was no definitely demonstrable invasion of the broad ligaments.

Operation. On January 10, under nitrous oxide anæsthesia, delivery of the cervix to the vulva was accomplished despite the markedly elevated position and limited mobility of the uterus. Extension of the growth was in close proximity to the bladder, but the latter could be separated and was mobilized and advanced 1½ inches higher on the uterus. A moderate treatment with surgical diathermy was administered to destroy the necrotic local growth.

Microscopic study revealed a richly cellular cancer containing many epithelial pearls and cells of varied size provided with abundant mitotic figures.

On February 16, the patient was re-examined, this time under ethylene anæsthesia. There was found gross evidence of remaining malignancy of the anterior lip extending rather deeply into the cervical canal and laterally somewhat into the left broad ligament. The sloughing surface of the tumor was well healed.

Surgical procedure and radiation. The bladder, which had returned to its normal position since the diathermy treatment, was readily mobilized and displaced upward. A circular incision around the cervix and blunt dissection of the vagina along natural lines of cleavage exposed freely the pillars of the bladder anteriorly, the broad ligaments and cellular tissues anterolaterally, and the pillars of the rectum posteriorly. The bladder was now sutured to the body of the uterus in its reflected position in order to keep it out of the way during radiation. Seven radium needles were inserted about the cervix, chiefly laterally into the bases of the broad ligaments. Seventy-five milligrams of radium in capsules, in tandem, were placed in the uterine canal. All told, a dosage of 3,000 milligram hours was given.

Postoperative course. The patient made an uneventful convalescence and left the hospital in a week. A notation on re-examination, April 20, 1933, reads as follows: "The cervix appears to be entirely healed and is freely movable. There is no evidence of remaining displacement of the bladder or of the reflected vaginal walls, no pelvic induration, nodulation or tenderness. The patient feels fine, has no vaginal discharge, no urinary or bowel symptoms, is gaining weight, has a splendid appetite and seems to be well on the way to a clinical cure."

CASE 2. Patient was admitted to Passavant Memorial Hospital December 15, 1932. She was a married woman of 46, formerly a graduate nurse. One pregnancy at the age of 18, terminated by spontaneous abortion in the fifth month. Menstruation had always been regular, of the 28 day type, duration 5 days, until the menopause one year ago, at the age of 45 years. Malaise and slight pelvic distress led the patient to insert a finger into the vagina 4 months prior to entrance into the hospital. She felt a mass but did nothing further until 3 weeks prior to entrance, at which time she palpated a nodulation "like a cauliflower." A dirty, blood tinged discharge now appeared and persisted, with increasing bloody flow as time progressed.

Physical examination revealed the patient to be in fairly good general condition; heart and lungs, negative; blood pressure, 130/80; red blood count, 4,160,000; leucocytes, 11,300; hæmoglobin, 70 per cent; Wassermann, negative. The pelvic findings are included in the detail of the operations recorded below.

Surgical diathermy treatment. On December 17, under nitrous oxide anæsthesia, the cervix was found to be enlarged to double normal size by a cauliflower-like necrotic tumor which involved the entire vaginal portion of the cervix and slightly invaded the vaginal wall in all directions. It was recorded that submucosal extension was apparently still more widespread than the surface growth and infiltration anteriorly had apparently progressed to the floor of the bladder, if not into it. "The generous sized uterus is freely movable although there must be some broad ligament invasion."

With painstaking delivery, the cervix was brought beyond the level of the vulva. Tissue was removed for biopsy.

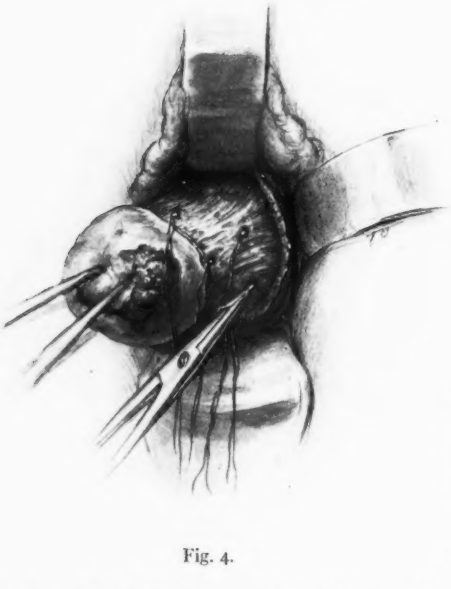

Fig. 4.

Fig. 5.

Fig. 4. The body of the uterus and the regions of the broad ligaments and cardinal ligaments are now well visualized. With the uterus partially delivered, vaginally, the bladder safely anchored in its elevated position with a catgut suture, and the paracervical tissues exposed, radium needles or radon seeds are now inserted where needed, as indicated, with assurance of safety of the adjacent vulnerable organs.

Fig. 5. Radium needles and chain tandem radium capsules in position. The placement of the needles is accurately portrayed in Figure 4.

Extensive surgical diathermy was given, moist gauze packing being employed to protect the adjacent tissues.

Histological study of the growth revealed an anaplastic epithelial cell carcinoma of the cervix.

Surgical procedure and radiation, January 17, 1933, ethylene anæsthesia. The diathermy treatment of a month previous, together with changes wrought by the cancerous growth, had resulted in complete destruction of the anterior cervix and a major portion of the posterior part. Slight dissection revealed the bladder lying on the uterine canal with almost no intervening tissue. The uterus was mobile. Extension of the growth anteriorly apparently had not involved the bladder, but it was much distorted and its separation and upward displacement without injury was accomplished only with difficult, painstaking dissection. Lateral and posterior dissection of the vagina was followed by further tedious complete separation of the bladder from the uterus, including opening of the anterior cul-de-sac. An excellent delivery of an apparently hopelessly entangled and distorted uterus was obtained. The remaining shrunken organ was only 2 inches in length. Some fibrosus and residual infiltration (apparently cancerous) persisted in the para-uterine cellular tissues, but evidently not beyond access of radiation now that the dissection had delivered the uterus and had displaced the vulnerable bladder and ureters. A palisade of 8 radium needles was inserted into the tissues around the cervix and into it and one 50 milligram tube of radium was placed in the uterine canal. A total of 3,000 millicuries was administered.

Rectovaginal examination, two and two-thirds months subsequently, April 5, 1933, revealed healing far progressed. The region of the uterus and its vicinity, which had been raw and necrotic during the interval following the operation, was now almost healed. The retracted tissues (still somewhat retracted a month earlier) now covered the stump nicely. The mobility of the uterus remained limited but the outlook appeared encouraging.

CASE 3. Patient was admitted to Passavant Memorial Hospital, November 2, 1931. She was 42 years of age, had previously been married, and had been divorced for 10 years. One birth, with normal delivery, occurred at the age of 21. Menstruation had always been regular, 28 day type, duration 4 to 6 days, with normal, painless flow until present trouble. Routine examination by a physician 3 months ago revealed a raw, ulcerated area on the cervix. No improvement with local treatments. She flowed persistently following regular period 1 month prior to entrance and thereafter bled rather freely, alternating with periods of spotting, until time of entrance.

Physical examination revealed a rather pale, fairly well nourished, somewhat nervous patient. Heart and lungs were negative; blood pressure, 116/66; red blood cells, 3,810,000; leucocytes, 8,550; hæmoglobin, 75 per cent.

Examination and radium treatment, November 3, ethylene anæsthesia. Although superficially limited, the friable, bleeding lesion near the external os of the cervix was found to be an extensive endocervical cancer, apparently originating within the cervical canal. The fundus was of generous size, retrodisplaced, mobile. Gentle removal of the endocervical cancerous débris left a cavity half the diameter of the cervix, beyond which the growth had apparently extended into the left parametrium. The prognosis appeared unfavorable. A palliative intra-uterine treatment with radium capsules was given.

Microscopic examination revealed a loose fibrous stroma containing islands of a squamous cell, group 3, "middle ripe" growth.

On January 26, 1932, the patient was again given ethylene anæsthesia. The fundus of the uterus was found to be large and mobile. There was a palpable thickening anterolaterally, on the left. The cervix was crateriform, the lower uterine segment slightly obstructed. Dilatation yielded some retained serohæmorrhagic fluid.

The bladder was separated from the cervix, displaced upward and anchored with one catgut suture. Eight radium needles were buried in a palisade encircling the cervix and 75 milligrams of radium in 2 capsules in tandem were placed in the canal. A total radiation of 1,750 millicuries was given.

Surgical exposure and radium treatment. The patient was kept under observation, with bimanual rectovaginal examination at monthly intervals. Her isolated social status and the need of a complete understanding of her condition because of her dependent child led to a frank discussion of the prognosis. The clinical course continued excellent but there remained an infiltration in the left parametrium. After prolonged temporizing, it was finally decided that radical intervention was preferable to expectancy; this, despite the fact that increasing infiltration could not be determined with certainty.

Operation, February 14, 1933, ethylene anæsthesia. As a result of the previous radium treatments, the uterus presented the appearance of a clinical cure. The external os was sealed, the canal 2¼ inches in depth, the size of the uterus normal. The bladder was flush with the cervix and there was considerable œdema in the region of the pillars. There was moderate uterine mobility, with some palpable "fullness" in the left parametrium.

The bladder was separated and displaced upward 2 inches. A circular incision around the cervix was followed by separation of the vaginal mucosa posteriorly and laterally, thus exposing the broad ligaments thoroughly and extending upward posteriorly to the pillars of the rectum. With the uterus thus mobilized and the bladder held up by a fixation suture, 7 radium needles were thrust into the left broad ligament, and high into the cervix anteriorly and less high posteriorly and laterally, all under digital control of the left hand, with the forefinger in the vagina and the midfinger in the rectum to protect against bowel injury. Seventy-five milligrams of radium in 2 capsules were placed in the uterine canal. A total radiation of 2,075 millicuries was given.

Postoperative course. The patient left the hospital after an uncomfortable week. There was no palpable exudate. A month later, the uterus was somewhat descended, heavy, "lumpy," raw, discharging, and apparently still uncovered by mucosa (speculum examination was avoided because of excruciating tenderness).

Very recently, 2 months after operation and radiation, the patient returned to the hospital because of pelvic distress. Speculum examination revealed considerable necrosis of the cervical portion of the uterus, and some of the adjacent parametrium. There was a rather free serous discharge containing fragments of débris. The bladder and ureters, apparently in excellent condition, had returned to normal position. The lateral vaginal walls were no longer retracted. Rectovaginal examination indicated a normal bowel and revealed no pelvic exudate, but some brawny fixation, and the patient experienced discomfort in the region of the rectosigmoid. Despite the rather extensive tissue destruction, which was more than anticipated or desired, it appeared that the process was subsiding without serious complication.

In view of the fact that these three patients have been cared for within the last several months, it is evident that a prognosis as to the ultimate outcome is unwarranted. Yet the fact that intensive radiation can be accomplished without injury to important structures must lead to a more encouraging outlook in cases of this character.

Complete surgical recovery has occurred in one of these cases, with accompanying gross disappearance of the growth and free mobility of a now apparently healthy uterus. A second patient has made an almost complete surgical recovery, except for some irregularity in contour of the uterus incident to partial destruction of the cervix and lower uterine segment. The third patient has, at the present time, some necrosis of the cervix and adjacent cellular tissues with considerable associated pelvic cellulitis and profuse discharge which contains some fragments of tissue. The bladder and ureters are in excellent condition despite the nearby destructive process; this bladder would undoubtedly have been injured by the radiation had it not been spared by preliminary dissection and retraction at the time of treatment.

The raw surfaces created by the dissection in these cases apparently need cause no concern. The dissected tissues gradually fall back into their normal positions after removal of the radium. The use of sutures is unnecessary. Even the bladder reflection, despite the anchoring suture of catgut which holds it in upward displacement during radiation, quickly resumes its natural position.

Further experience may require modification in the detail of the procedure. We are most concerned with the value of the underlying principles involved.

It has been thought by some that implantation of radon seeds into the cancer bearing pelvic tissues at the time of abdominal operation may prove to be a decided asset in our fight against cancer. Gellhorn has made intra-abdominal implantations of radon, under guidance of the other hand, within the vagina. He then closes the abdomen and makes the usual vaginal introduction of radium. Perhaps intra-abdominal placement of radon may be advantageously employed in conjunction with the procedure herewith suggested.

CONCLUSIONS

1. The feasibility of coincident surgical exposure and radium therapy in the treatment of extensive cervical cancer has been demonstrated in three cases.

2. It is my belief that acceptance of the principle of combined vaginal approach and appropriate radium therapy will result in an improved prognosis in many relatively extensive cases of carcinoma of the cervix which have heretofore had a dubious outlook.

THE TREATMENT OF DUODENAL FISTULA

Including a Report of Two New Cases and a Report of a New Buffer Solution

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ANY surgical complication having a reported mortality of 50 per cent must of necessity be studied carefully. Furthermore, when death may supervene 1 or 2 days after the complication arises, it certainly behooves the surgeon to be well acquainted with its diagnosis and the various kinds of treatment, so that he may start the most efficient treatment immediately. A patient with duodenal fistula becomes debilitated with extreme rapidity by inanition, dehydration, and the loss of chlorides. It becomes one of the most ravaging and one of the most disconcerting conditions with which the gastro-intestinal surgeon has to deal. It inspires dread both because of its high mortality and its extremely rapid course.

An attempt is made in this paper to review the literature on the subject since 1865—94 cases—and to add 2 of our own, making a total of 96 cases. This is the largest series of cases reported in any paper so far. There are but few reports of the condition before 1900. When recognized, it was dealt with haphazardly, and the results were consequently poor. We found no case with recovery reported in medical literature before 1900. During this period, the treatment was medical and altogether conservative. Possibly for this very reason, the treatment became surgical for the next 25 years. The mortality rate, which had been 100 per cent, dropped to between 43 and 50 per cent. Since 1927, the treatment has again become medical but based on radically different principles. The mortality rate has dropped markedly. The late reports on the present treatment are so good that it may become the treatment of choice, since at least one good sized series shows 100 per cent recovery.

Lilienthal reported the first two cases of duodenal fistula treated by surgical means, in 1901. Two years later, von Cackovic collected 6 additional cases from the literature, all of whom died after having been treated conservatively. In 1917, Melchoir reported on 14 cases, while Colp reviewed 53 cases in the literature and added 8 of his own in 1923. In the same year, Cameron reported on 29 cases. In 1929, Potter (50) reported on a series of 9 cases treated medically with no deaths. These various reports seem to prove that duodenal fistula is not so rare a condition as one might at first conclude. The success of recent medical treatment definitely disproves the view of Pannet, who stated that "duodenal fistula never healed without surgical aid and if left was invariably fatal."

Duodenal fistula may result from various causes and the point of exit may be almost anywhere on the abdomen or on the back. Trauma of the duodenal wall may result in necrosis and abscess, which in turn may gravitate and rupture far from its origin. In Forster's case of retroperitoneal perforation, the pus ascended along the great vessels and localized in the neck. Wagner and Fenwick cite cases in which the burrowing fluid localized in the inguinal region and autopsy proved the connection with the retroperitoneal second portion of the duodenum. Other such cases are cited by Koerte, Esau, and Hinton (25). Quite often the fistula is the result of operative interference on or near the duodenum. The wall of the duodenum may become traumatized or its blood supply compromised. Mayo (39) cited 3 cases in which the duodenal wall was injured in performing right nephrectomies. Other cases are cited by von Cackovic, Payr, and Thevenard. The duodenum may also be injured easily in dissecting away adhesions during gall-bladder operations. Such cases were recorded by Fink, Meyer, and Merk. Fistula may also follow accidental opening of the duodenum or transduodenectomies for the extraction of stone in the common bile duct. Various types of resection of the stomach may be followed by fistula as is shown by the cases cited by Melchoir, Makkas, Kelling, and Cameron.

Perforated duodenal ulcer, when this condition has been treated with simple suture, is another very common cause of duodenal fistula. The greatest care must be taken that the suture lines are perfect. A minute leak will enlarge shortly and result in fistula. The natural activity of the stomach and duodenum encourages such a result. As the stomach empties its contents into the duodenum, the duodenal pressure is greatly increased and sutures cut through the brittle wall. Many such cases are cited in Table I.

Gauze packing is one of the most important contributing factors in the formation of duodenal fistula. Particular stress was laid on this point by

Cameron. In this location, there is a great deal of œdema of sutured tissue. Gauze packs increase this œdema, possibly to the point of interfering with the circulation. There may be also a slight adherence between the sutures and the gauze. Then, upon the removal of the gauze, naturally slight pulling on the sutures results and this would in turn result in some enlargement of one or more suture openings. Even such a small opening may become enlarged rapidly by the action of the trypsin of the pancreatic juice and become the starting point of a fistula. Furtwangeler stated that most severe forms of fistula resulted from leaking sutures.

Infection of the suture lines is undoubtedly another contributing cause. This is especially true in cases of ruptured duodenal ulcer. Infection prepares the way for leaking sutures and for perhaps rupture of the entire suture line by increasing the œdema and by rendering the bowel wall more brittle. Due to their injury, the tissues are below par. Their blood supply is compromised. The natural local resistance of the tissue is greatly lessened due to this lessened nutrition.

The strong digestive action of the pancreatic trypsin is the most important primary cause of duodenal fistula. It attacks the proteins of the living tissues and is highly destructive. It is this ferment that seeps through small suture leaks and rapidly enlarges them. Furthermore, there is no healing while the trypsin remains active in the wound. The whole wound usually breaks open and rapidly enlarges. Potter stated, in his discussion of the digestive activity of the fistular fluid, that the bile played a minor rôle, although it did attack the fat of the abdominal wall. The trypsin was by far the most damaging, he stated.

The diagnosis offers no great difficulty in the great majority of cases, especially if the complication of duodenal fistula is kept in mind. According to Table I, the time of onset may vary from 2 days to several months. On the average, the time of onset is from 5 to 14 days. Oftentimes the onrush of the fistular fluid follows the gauze pack as it is removed. When the tryptic fluid has once broken through, the onset of the fistula is very rapid and the amount of fluid coming through may be enormous. The operative wound usually breaks open along its entire length. The wound becomes extremely tender, and the skin around the wound edges becomes inflamed and bleeding. Most patients complain of a feeling of severe burning in the entire wound and the adjacent skin surface. The fat in the adipose layer becomes digested and the wound takes on an excavated appearance. The walls of the blood vessels along the margin of the wound may become digested and bleeding from the wound may be of alarming proportions. The chemical reaction of the fluid discharge is usually strongly alkaline in the worst type of fistula. Should the fluid discharge be acid in reaction, the fistula is probably suprapapillary in origin.

There seems to be considerable variation in the destructiveness of various fistulas and in the toxæmia accompanying them. This, of course, depends on the size of the fistular opening and the tortuosity of the tract. The point in the duodenum where the fistula originates is another very important factor. It is either suprapapillary or infrapapillary according to whether it is above or below the papilla of Vater. This distinction is of great prognostic value, since suprapapillary fistulas certainly are not nearly so destructive as those originating below the papilla of Vater. However, fistulas that follow the Billroth II type of operations usually contain bile and these fistulas are excellent examples of the suprapapillary type. It is also well known that pancreatic ferments may be carried retrograde by antiperistaltic waves of the duodenum. Payr reported an infrapapillary fistula with absence of bile and pancreatic ferment in the secretion.

The type of duodenal origin of the fistula probably has a great deal to do with the amount of the discharge. It is easy to conceive that if the origin is well down along the lateral wall of the duodenum, there would be more resistance to the escape of fluid than would be the case if the opening were situated on the anterior wall. Either a right or left sided opening would have a tendency to a valve-like effect. But no matter where the opening, the fact remains that a duodenal fistula greatly excites the stomach to activity. The intestinal law of Bayliss-Starling states that stimuli applied to the duodenum produce a muscular excitation in oral direction and a muscular relaxation in aboral direction. Barsony and Hortobagyi also showed that experimental duodenal fistula greatly increased the muscular activity of the stomach. This was shown graphically in their experiments.

The prognosis of duodenal fistula is always grave. The duodenum has its own succus entericus and also receives the bile, the gastric contents, and the powerful pancreatic secretions. A fistula, therefore, causes loss of intestinal juices and all foods and fluids ingested. It is like turning off a mill race suddenly. Inanition, dehydration, and exhaustion comes on with extreme rapidity. The introduction of fluids rectally, intravenously, and by hypodermoclysis control

TABLE I.—GENERAL DATA, VARIOUS TREATMENTS, AND FINAL RESULTS

Surgeon Date	Diagnosis	Operation	Type of drainage	Time of appearance of fistula	Type of treatment	Length of life after treatment was instituted	Final result
Krauss 1865	Perforated duodenal ulcer	None	?	?	Conservative	1 month	Died
Hinton 1866	Rupture of duodenum	None	?	Several mos. later	Conservative	20 years	Died
Rintel 1867	Intestinal tuberculosis	None	?	2 days	Conservative	30 days	Died
Luneau 1870	Perforated duodenal ulcer	None	?	90 days	Conservative	18 months	Died
Fenwick 1900	Rupture of duodenum	None	?	42 days	Conservative	6 months	Died
Kraske 1901	Cholelithiasis	Choledochotomy	Tamponade	2 days	Attempted suture	1 month	Died
Merk 1902	Cholecystitis	Choledochotomy	Tamponade	15 days	Conservative	70 days	Cured
Cackovic Von 1903	Sarcoma	Nephrectomy	Tamponade	10 days	Jejunostomy 17 days	19 days	Died
Koerte 1904	Rupture of duodenum	Suture	Tamponade	60 days	Suture. Jejunostomy 5 weeks	2 days	Died
Mayo 1904	(1) Perforated duodenal ulcer	Suture, gastro-enterostomy	Tamponade	?	Conservative	?	Died
	(2) Perforated duodenal ulcer	Suture	Tamponade	?	Conservative	Healed	Cured
Fink 1905	Cholelithiasis	Cholecystectomy	Tamponade	28 days	Gastro-enterostomy and suture at 35 days. Perforation and re-suture	?	Cured
Kehr 1905	(1) Cholecystitis	Cholecystectomy	Tamponade	8 days	Conservative	22 days	Cured
	(2) Cholelithiasis	Cholecystectomy	Tamponade	5 days	Suture at 11 days	Recurrence 11 days healed 16 days	Cured
	(3) Cholelithiasis	Cholecystectomy	Tamponade	6 days	Suture 9 days	Suture 3 times gastro-ent. 17 days	Died
	(4) Cholelithiasis	Cholecystectomy	Tamponade	20 days	Conservative	43 days	Cured
	(5) Cholelithiasis	Cholecystectomy	Tamponade	12 days	Conservative	18 days	Cured
Wagner 1906	Perforated duodenal ulcer	None	None	8 months	Conservative	15 months	Died
Berg 1907	(1) Carcinoma pancreas	Cholecyst-duodenostomy	?	5 days	Ant. gastro-ent. with pyloric occlusion	Discharge stopped at once. 67 days cured	Died of ca.
	(2) Perforated duodenal ulcer	Suture of perforation	?	7 days	Post. gastro-ent. fistula sutured	Recurrence 3 days pylorus occluded	Died
Makkas 1907	(1) Carcinoma of stomach	Billroth I	?	10 days	Suture 5 days	1 day	Died
	(2) Pyloric tumor	Billroth I	?	2 days	Conservative	1 month	Died
	(3) Stomach tumor	Billroth II	Tampon	6 days	Conservative	10 days	Died
Knaggs 1908	Perforated duodenal ulcer	Incision of psoas abscess	None	Several weeks	Post. gastro-ent. pyloric occlusion 3 months	At once	Cured
Cameron 1908	?	?	?	?	Post. gastro-ent. Pyloric occlusion	Healed at once	Cured
Rigby 1911	(1) Renal tuberculosis	Nephrectomy	?	Few weeks	Conservative	Healed	Cured
	(2) Perforated duodenal ulcer	Drainage of abscess	Tampon	3 days	Conservative	9 days	Cured

TABLE I.—GENERAL DATA, VARIOUS TREATMENTS, AND FINAL RESULTS—Continued

Surgeon Date	Diagnosis	Operation	Type of drainage	Time of appearance of fistula	Type of treatment	Length of life after treatment was instituted	Final result
Esau 1911	Nephrectic abscess	Nephrectomy	Tampon	3 days	Jejunostomy	6 days	Died
Telford 1912	Perforated duodenal ulcer	Incision of abscess	Tampon	5 days	Suture and gastro-enteros.	6 days	Died
Winiwarter 1912	Rupture of duodenum	Suture	Tampon	2 days	Enterostomy	2 days	Died
Struthers 1913	Ruptured duodenal ulcer with fistulas (3 cases)				Conservative (ulcers not closed)		All three died
Souttar 1913	Perforated duodenal ulcer	Suture and post. gastro-enterostomy	?	?	Post. gastro-ent. pyloric occlu.	Recovered	Cured
Thevenard 1913	?	Nephrectomy	?	?	Gastro-enterost. Beck's paste	9 days	Cured
Turner 1913	(1) Perforated duo. ulcer	Duodenorrhaphy	Tampon	2 days	Conservative	8 days	Died
	(2) Cholelithiasis	Cholecystectomy	Tampon	3 days	Conservative	3 days	Died
Mayo 1914	(1) ?	Nephrectomy	?	5 days	Conservative	14 days	Died
	(2) Carcinoma of kidney	Nephrectomy	?	5 days	Conservative	10 days	Died
	(3) ?	Nephrectomy	?	?	Conservative	14 days	Died
	(4) Kidney stone	Nephrectomy	Tampon	2 days	Suture at once	Healed	Cured
Melchoir 1914	Carcinoma of stomach	Billroth I	Tampon	12 days	Conservative	Healed in 2 years	Cured
Pannet 1914	Perforated duodenal ulcer	Duodenorrhaphy	Tampon	5 days	Jejunostomy	Healed 15 days	Cured
Cheever 1915	Ruptured duodenal ulcer	Duodenorrhaphy	Tampon	5 days	Irrigation	Healed 11 days	Cured
Davis 1918	Duodenal-ureteral fistula	Nephrectomy	?	4 days	Conservative	Healed 8 days	Cured
Gardner 1918	Gall stones	Cholecystectomy	?	9 days	Conservative	Healed 1 month	Cured
Palmer 1918	(1) Carcinoma of stomach	Billroth II	Tampon	8 days	Conservative	Healed 24 days	Cured
	(2) Gall stones	Cholecystec. duodenorrhaphy	Tampon	6 days	Conservative	Healed 28 days	Cured
Einhorn 1918	(1) Biliary fistula	Closure	?	17 days	Duodenal tube per os	Healed 17 days	Cured
	(2) Cholecystitis	Cholecystectomy	Tampon	21 days	Duodenal tube jejunal feeding	Healed 5 months	Cured
Clark 1919	(1) Cholecystitis	Cholecystectomy	Tampon	17 days	Conservative	Healed 20 days	Cured
	(2) Cholecystitis	Cholecystectomy	?	3 days	Jejunostomy	Lived 2 days	Died
Hendon 1919	Cholangiitis	Exploratory	Tampon	At once	Conservative	Healed 5 weeks	Cured
McGuire 1919	Cholecystitis	Cholecystectomy	?	9 days	Jejunostomy	Healed 3 weeks	Cured
Meyer 1920	Cholecystitis	Cholecystectomy	Tampon	?	Conservative	Healed 7 months	Cured
Erdmann 1921	Duodenal rupture	Duodenorrhaphy	Tampon	6 days	Jejunostomy	Healed 18 days	Cured
Stadler 1921	Rupture of gall bladder	Drained abscess	Tampon	5 days	Olive oil tampon	Healed 1 month	Cured

TABLE I.—GENERAL DATA, VARIOUS TREATMENTS, AND FINAL RESULTS—Continued

Surgeon Date	Diagnosis	Operation	Type of drainage	Time of appearance of fistula	Type of treatment	Length of life after treatment was instituted	Final result
Furtwangeler 1922	Blow on abdomen	Abscess broke spontaneously	No	5 weeks	Post. gastro-ent. pyloric occlusion	Lived 8 days	Died
Colp 1923	(1) Cholelithiasis	Choledochotomy, duodenorrhaphy	Drainage	5 days	Gastro-enteros. pyloric occlusion	Lived 8 days	Died
	(2) Cholelithiasis	Choledochotomy, duodenorrhaphy	Drainage	7 days	Gastro-enteros. pyloric occlusion	Lived 1 day	Died
	(3) Cholelithiasis	Choledochotomy	Drainage	20 days	Conservative	Healed 43 days	Cured
	(4) Cholelithiasis	Left hepatoduodenotomy	Drainage	16 days	Gastro-enterostomy with pyloric occlusion	Lived 2 hours	Died
	(5) Cholelithiasis	Cholecystectomy duodenorrhaphy	Drainage	7 days	Gastro-enterostomy, pyloric occlusion, jejunostomy	Lived 20 days	Died
	(6) Cholecystitis	Choledochotomy	?	?	Conservative	Healed 4 months	Cured
	(7) Cholecystitis	Cholecystectomy, duodenorrhaphy	Drainage	5 days	Conservative	Healed 20 days	Cured
	(8) Abdominal pain	Duodenorrhaphy	Drainage	5 days	Conservative	Lived 40 days	Died
Cameron, A. L. 1923	Gastrectomy	Anterior Pólya	Soft rubber drains	7 days	Used continuous suction 11 days	Healed 11 days	Cured
Gaminara, A. 1923	Pyloric neoplasm	Billroth II	?	10 days	Syphonage 12 days	Healed	Cured
Ronaldi, A. 1923	Cholecystitis	Cholecystectomy duodenum opened	Packing	At once	6 weeks	Healed	Cured
Pignatti, A. 1924	Pyonephrosis	Nephrectomy	?	15 days	Conservative	Lived 1 month	Died
Rigby 1924	(1) Perforated duodenal wall	Sutured and covered with omentum	Rubber tube	7 days	Post-gastro-enterostomy duodenal occlusion	30 days	Cured
	(2) Right pyonephrosis	Nephrectomy	?	2 days	Conservative	60 days	Cured
	(3) Ruptured appendix	Appendectomy	Two tubes and gauze	3 days	Conservative	21 days	Cured
	(4) Duodenal diverticulitis	Removal of gangrenous diverticulum	Gauze drainage	3 days	Conservative	14 days	Cured
	(5) Subphrenic abscess	Drainage	Drainage	At once	Sutured	At once	Cured
	(6) Cancer of stomach	Partial gastrectomy	?	22 days	Conservative	9 days	Cured
	(7) Cancer of stomach	Partial gastrectomy	?	23 days	Conservative	5 weeks	Cured
Webb, C. W. 1925	Peptic ulcer	Post-gastro-enterostomy	Drainage	18 days	Conservative	16 days	Cured
Lick, Maxwell 1925	Perforated duodenal ulcer	Suture and postgastro-enterostomy	Cigarette drains	3 days	Drainage by suction	8 days	Died
Ahrens 1925	Ovarian cyst, appendicitis	Ovarectomy appendectomy	Bowel opened accidentally	At once	Inserted rubber tube	4 weeks	Cured
Alexander 1926	Perforated duodenal ulcer	Suture	Drainage	9 days	Conservative	16 days	Cured
Gibby, Hubert 1926	Gall stones	Cholecystectomy	?	4 days	Sutured twice omentum used	1 week	Cured
Johanson 1927	(1) Cholecystduodenostomy	?	?	?	Injected 1 per cent citric acid	10 days	Cured
	(2) Cholecystitis	Cholecystectomy	?	30 days	Injected 1 per cent citric acid	90 days	Cured
Potter 1927	Ruptured gastric ulcer	Suture of ulcer	Soft drains	9 days	Unsuccessful closure. Suction. HCL, beef juice, olive oil	30 days	Cured

TABLE I.—GENERAL DATA, VARIOUS TREATMENTS, AND FINAL RESULTS—Continued

Surgeon Date	Diagnosis	Operation	Type of drainage	Time of appearance of fistula	Type of treatment	Length of life after treatment was instituted	Final result
Potter C. 1929	(1) Perforated duodenal ulcer	Appendectomy suture	Large drains	At once	HCL 1/10 normal, buffer solution of olive oil and beef juice	26 days	Cured
	(2) Perforated duodenal ulcer	Ulcer inverted	Large drains	8 days	HCL 1/10 normal, buffer solution of olive oil and beef juice	11 days	Cured
	(3) Pus tubes and abscess	Drainage	Large drains	4 days	HCL 1/10 normal, buffer solution of olive oil and beef juice	Healed	Cured
	(4) Appendicitis and obstruction	Jejunostomy	Large drains	At once	HCL 1/10 normal, buffer solution of olive oil and beef juice	Healed	Cured
	(5) Appendiceal abscess	Jejunostomy	Large drains	At once	HCL 1/10 normal, buffer solution of olive oil and beef juice	20 days	Cured
	(6) Cholelithiasis	Cholecystectomy jejunostomy	?	At once	HCL 1/10 normal, buffer solution of olive oil and beef juice	Healed	Cured
	(7) Gastric and duodenal ulcer	Partial gastrectomy	?	7 days	Used acetic acid	36 days	Cured
	(8) Intestinal obstruction	Enterostomy	?	At once	Used acetic acid 2 weeks then HCL	8 weeks	Cured
Worthen 1930	Perforated duodenal ulcer	Attempted closure	?	?	Conservative for 7 mos. then suture	11 days	Cured
Kittelson 1932	(1) Acute appendicitis	Enterostomy	Drainage	At once	1/10 normal HCL, lactone milk for buffer solution	11 days	Cured
	(2) Cholecystitis	Cholecystectomy	Drainage	5 days	1/10 normal HCL, lactone milk for buffer solution	19 days	Cured

the situation only partially. The toxic intestinal contents are undoubtedly absorbed along the fistulous tract. Studies of intestinal obstruction have shown that the pancreatic juice is very toxic —much more so than the contents of the cæcum.

This toxæmia has been very well described by Haden and Orr, Potter, and Walters. They stated that it was the result of rapid dehydration, due to the large volume of fluids lost and to the rapid depletion of chlorides. These factors caused an increasing alkalosis, characterized by decreasing concentration of blood chlorides and progressive increase of blood urea. Walters concluded that the main cause of the toxæmia was the loss of the protective action of the chlorides of the digestive juices, which were discharged through the fistula. He thought that this loss turned the tide of neutrality of the blood toward alkalinity. He stated further that any toxic state is accompanied by increasing blood urea, due in some cases to the production of a nephritis which prevents the elimination of urea. At times it may be due to an abnormal amount of urea formed from the breaking down of body tissues. Potter stated that the toxæmia associated with duodenal and fæcal fistula is practically the same as that associated with intestinal obstruction.

As shown in Tables II and III, the treatment of duodenal fistula has a mortality of 35.8 per cent. However, separating the two major types of treatment, surgery has a mortality of 50 per cent, while the conservative treatment has a mortality of only 27.7 per cent. W. J. Mayo closed one case of posterior fistula successfully while Cameron cited five failures in six attempts. The toxæmia present in these patients is so severe that if operative procedures are resorted to before they at least have partially recovered, a fatal outcome is almost a certainty. Of the surgical procedures, simple closure, jejunostomy and enterostomy, carries the least mortality. Posterior gastro-enterostomy together with simple closure or combined with pyloric occlusion shows 7 deaths to 6 successful outcomes. Posterior

TABLE II.—RESULTS OF VARIOUS KINDS OF CONSERVATIVE TREATMENT

Treatment	Cases cured	Deaths
1. Ointments, applications, dressings	27	19
2. Olive oil tampon	1	0
3. Irrigations	1	0
4. Duodenal tube per os	2	0
5. Hydrochloric, acetic, or citric acid	11	0
6. Drainage by suction or syphon	3	0
7. Use of T shaped rubber tube	1	0
Totals	46	19
Per cent	72.3	27.7

Grand total of 65 cases treated conservatively.

TABLE III.—RESULTS OF VARIOUS TYPES OF SURGERY PERFORMED ON DUODENAL FISTULA

Kind of operation	Cures	Deaths
1. Simple suture	5	4
2. Jejunostomy	3	4
3. Enterostomy	0	1
4. Gastro-enterostomy and suture	1	2
5. Gastro-enterostomy and Beck's paste	1	0
6. Gastro-enterostomy and pyloric occlusion	5	4
Totals	15	15
Per cent	50	50

Grand total of 30 cases treated by surgery.

gastro-enterostomy with pyloric occlusion was first practiced by Berg and has proved successful in stopping the discharge at once. Jejunostomy is a great aid in stopping the discharge and is not nearly so dangerous. Direct closure of the fistula has been tried many times but the sutures usually fail to hold and the fistula recurs.

Einhorn (11) employed the use of the duodenal tube in 2 cases successfully. In one of his cases the tryptic action was very marked. The tube was introduced *per os* and was kept in place for 2 days. It supplied food and water in abundance at small risk and lessened the discharge markedly. However, the duodenal tube can not be used in cases of pyloric obstruction and in cases of resections of the stomach of the Billroth II type.

A constipating diet has been advocated. It is given with the idea of solidifying the intestinal contents and thereby lessening the flow of fluid through the fistula. Boiled milk has been used for the same reason. However, the nausea and vomiting associated with the toxæmia oftentimes renders any kind of feeding difficult. Rectal feeding is of some help, but usually the time of healing is too long and the body weight can not be kept up. Oral administration of opium has been given to lessen the peristaltic action of the bowels.

Attempts have been made to dilute the trypsin. Cheever used a continuous stream of water to which had been added an alkali. He stated that the results on the fistula were good but that he had to discontinue its use because of irritation to the skin. Palmer also diluted the discharge with water to which he had added an alkali. There are other numerous references in the literature to attempts of healing the fistula by increasing the alkalinity of the discharges. Perhaps the minds of these workers were influenced by the fact that gastric ulcers heal under alkaline therapy.

Continuous suction was first used by Jones and Williams. Cameron used continuous suction on a case in 1923 with good results and Lahey used this method in 1924. It has certain very definite advantages. The wound is kept fairly dry and this lessens the irritation in the wound and in the fistulous tract very much. The patients are much more comfortable locally. However, the loss of intestinal fluids is just as great as before. The toxæmia, being dependent on the loss of chlorides and a beginning alkalosis, would probably not be influenced very much. The method is of value in cases in which the fluid loss is moderate and the toxæmia of mild degree. The general condition of Cameron's case was good at all times and the fluid loss moderate.

It remained for Caryl Potter, in 1927, to introduce a marked improvement in the conservative treatment of duodenal fistula. He first acidified the discharge by adding one-tenth normal hydrochloric acid in a continuous stream deep into the fistula. He then packed the wound with gauze which he kept soaked with a mixture of olive oil and beef extract. In other words, he first attempted to inactivate the trypsin by acidification and, then, supplied a buffer solution on which the bile could act without attacking the living tissues. There was also protein in the buffer solution to neutralize whatever trypsin might not have been acidified by the hydrochloric acid and thus rendered inactive. By these means he was able to stop the digestive action of the discharges at once and gave the fistula a chance to heal. He supplied fluids and dextrose abundantly, as well as neutrient enemas. By these means the toxæmia and the starvation were held in abeyance while the fistula healed. In 1929, he reported 9 cases which had been treated with this method with no deaths. This is the largest and the most successful series of cases treated by any one method.

Warshaw and Hoffman, in 1930, treated a case successfully using Potter's method with a slight variation in buffer solution. They used a 10 per cent solution of Witte's peptone instead of Potter's mixture of beef juice and olive oil. They stated that they preferred the peptone solution

because of its greater ease of preparation. They also named three other solutions that might be used: egg albumen, protein milk powder, and French glue.

In my 2 cases, the trypsin was acidified and thus rendered inactive by allowing one-tenth normal hydrochloric acid to run deep into the fistula by means of a catheter. The wound was then kept packed with gauze which contained within it a second catheter supplying the gauze with the buffer solution, according to the arrangement of Warshaw and Hoffman. Each catheter ran back to a container, one for the hydrochloric acid and one for the buffer solution. The buffer solution used was whole lactone milk and this proved very satisfactory. It was prepared as follows: Whole milk was taken and re-pasteurized. Then this milk was cultured with stock culture of Bacillus acidophilus and kept warm for 6 hours, when it was quite thick. It was then placed in the container and used as a buffer. It was determined to try this after reading the work of Charles E. North on the beneficial action of lactic acid bacteria in the treatment of chronic fistula. The effect of the treatment was noticed immediately. The digestion of the tissues stopped at once and the pain ceased. The wound started to granulate. The fluid loss became less and less. The toxæmia, which had been increasing rapidly, seemed to have improved almost over night. The two fistulas healed in 14 days and 3 weeks, respectively. This treatment was supported by milk and egg enemas and by large amounts of fluid by the intravenous route as well as by hypodermoclysis.

SUMMARY AND CONCLUSIONS

An analysis of the 96 cases of external duodenal fistula reported in this paper shows that in 30 cases the fistulas followed operations on the gall bladder, in 22 cases operations for perforated duodenal ulcer, in 8 cases after nephrectomy, in 8 cases after resections of the stomach for malignancy, in 7 cases after operation, for acute appendicitis with obstruction, in 6 cases after rupture of the duodenum, and in 7 cases from other causes. Sixty-five patients were treated conservatively with a mortality of 27.7 per cent and 30 patients were treated by surgery with a mortality of 50 per cent. The mortality for the whole group, including all types of treatment, was 35.8 per cent.

In view of these statistics, it is seen that the prognosis of duodenal fistula is grave. The prognosis is most favorable when the fistula follows cholecystectomy, when it is 26.7 per cent. Fistulas following nephrectomies have had the highest mortality in this series, namely 80 per cent. Those following ruptured duodenal ulcer come next with a mortality of 50 per cent.

The statistics gathered seem to show that surgery in duodenal fistula has had its best results when used either very early or else very late. Conservative methods have had the best results. Potter's treatment, namely rendering the trypsin inactive by acidifying it by one-tenth normal hydrochloric acid and supplying buffer solutions containing fats and proteins, has so far had perfect results. It seems that this treatment will become the treatment of choice.

Numerous buffer solutions have been used and have proved their value. Such solutions should contain fat and protein. A new buffer solution is offered to the profession, namely whole milk thickened by the addition of Bacillus acidophilus. It was easily prepared and was used with complete success in my 2 cases.

REPORT OF CASES

CASE 1. Mrs. M. O., a white woman aged 45 years, had been well until she suddenly developed severe abdominal pain. Her family physician thought she was suffering from constipation and prescribed castor oil and enemas. She was seen by me 36 hours afterward, and was then extremely sick. Her temperature was 104.5 degrees, pulse 120, respiration 26. The abdomen was distended, rigid, and very tender throughout. She was vomiting fæcal material. A mass could be palpated in the region of the lower right rectus and the cul-de-sac was tender and boggy. A preoperative diagnosis of acute appendicitis, probably ruptured, was made.

At operation a ruptured gangrenous appendix was found. The pus cavity extended from the hepatic flexure to the pelvis. The small bowel was very much distended and it was evident that there was obstruction present. The appendix was removed without purse string suture and the cavity drained. An enterostomy was performed on the presenting loop of bowel, a No. 26F. catheter being used. The abdomen was then closed with drainage.

The convalescence was rather stormy for the first 4 days, then quieted down, and the patient seemed to get along very well. Considerable pus drained from the wound and gas and fæcal material drained from the enterostomy tube. The bowels moved and the enterostomy tube was removed. Then, on the thirteenth day after operation, the wound was wet and very tender. The patient complained of a burning sensation in the wound. The dressings were stained yellow and had an acrid odor. In 12 hours the whole wound had broken open and had almost doubled in size in 24 hours. The patient was very toxic and at the end of 24 hours was semi-stuporous. The amount of liquid coming from the fistula was so copious that the dressings had to be changed every 15 minutes. It was determined to use Potter's treatment and the wound was dressed accordingly. The beef juice and olive oil mixture used by Potter was found to be rather difficult to prepare so whole lactone milk was substituted. This was whole milk which was thickened by infecting it with Bacillus acidophilus. The treatment was found to be very effective. In a very short time the pain in the wound had stopped. Soon thereafter the slough had loosened and

healthy granulation appeared, and healing went on quite rapidly. The amount of the discharge grew less and the fistula had closed 11 days after this treatment was instituted. The treatment was supported by milk and egg enemas, glucose intravenously, and hypodermoclysis of normal saline. The normal saline seemed especially effective in counteracting the toxæmia, which was extreme in this case.

CASE 2. Mr. S. N., a white man aged 51 years, had had stomach trouble for about 15 years, which had been diagnosed chronic cholecystitis. The attacks of pain had been very severe, requiring at times 1 grain doses of morphine for relief. The present attack had lasted about 8 hours and the pain had been continuous. He had also nausea and vomiting. The bowels had moved shortly after the attack had started.

The temperature was found to be 103.5 degrees, pulse 130, and respiration 30. The abdomen was extremely tender and rigid and the patient had a peritonitic fæcies. A diagnosis of acute abdomen, with possibly a gangrenous gall bladder, was made.

At operation the gall bladder was found to be acutely inflamed, and a stone was protruding from the common duct. On account of the severe inflammation present, it was thought best to drain the gall bladder. Soft rubber drains were put down to the common bile duct, after the rent had been sewed up and covered with a piece of omentum. The abdomen was then closed with this drainage in place.

The temperature during the first few days after operation was quite high and the patient was quite toxic. However, the bowels moved and he was getting along fairly well, everything considered. The drains outside the gall bladder were removed on the fifth day, when it was noticed that there was some yellow fluid exuding from the wound. The patient complained of an itching and burning sensation in the wound. The next day the skin around the wound was excoriated and some fatty slough was present. The discharge was alkaline in reaction. A diagnosis of duodenal fistula was made and Potter's treatment instituted with whole lactone milk as a buffer solution. Atropine sulphate was given hypodermically every 6 hours in 1/200 grain doses. Supportive treatment of egg and milk enemas were given as well as normal saline intravenously and by hypodermoclysis. The fistula looked better after the first 24 hours and healed uneventfully in 19 days. The amount of discharge in this case was not so large as in Case 1, but it was copious.

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FRACTURES OF THE FEMUR

Report of Three Hundred and Eight Cases

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FRACTURE of the femur is recognized as one of the most difficult fractures to treat. Perfect results are hard to obtain. The duration of even temporary disability incident to such an accident is long and the mortality is high due to the fact that the patient is not infrequently well advanced in age. Fracture of the femur is not rare, especially in the large cities. In Charity Hospital, New Orleans, during the 2 year period from May 31, 1929, to May 31, 1931, there were 308 cases of fracture of the femur in an in-patient total of 81,350, an incidence of 1 in 264.14.

This paper is the report of a study of these 308 cases. The patients were treated in various wards and by a number of different men, who used a variety of methods. Seventy-nine of the 308 cases were treated in our wards.

AGE

The first decade furnished far more fractures of the femur in this series than did any other decade; 70 cases, or 22.7 per cent of the total. The eighth decade was the second largest contributor with 47 cases, or 15.2 per cent. In the second decade were scarcely less, 41 cases, or 13.3 per cent. Thirty-six per cent of the cases of fracture of the femur were in patients less than 20 years of age. The patients were 50 years or older in 41.88 per cent of the cases.

SEX

One hundred and ninety-two of the patients were males; 115 were females. In one instance, the sex could not be determined from records. The ratio of males to females was 1.67 to 1. Apparently as may be seen from Tables I, II, and III, females are more susceptible than males to the injuries (falls) which produce fracture of the femur late in life. Even though there are more males than females in this series, there are more females than males after the age of 60. This is accounted for by the proportionately greater number of females who sustain a fracture of the neck or the intertrochanteric region of the femur after the age of 60.

SITE OF FRACTURE

In Table IV, the fractures are divided according to their location and distribution in the different decades. We make no separate class for pertrochanteric fractures. There was no case of separation of the lower epiphysis of the femur in this series, nor was there a case of fracture of the lesser trochanter alone. Not infrequently, there was separation of the lesser trochanter associated with intertrochanteric fracture. In fractures of the middle third, we classify not only those fractures within the confines of the middle third of the shaft but also fractures at the junction of the middle and upper thirds or middle and lower thirds. Fractures of the upper third include those occurring in the shaft between the subtrochanteric region and the junction of the upper and middle third of the shaft, and fractures of the lower third include those in the shaft above the supracondylar region and below the junction of the middle and lower thirds.

In the earlier decades of life, most fractures of the femur occur in the middle third of the shaft. One hundred and forty-one (45.8 per cent) of the patients had fractures in the middle third of the shaft. Moreover, in 7 cases (5 per cent) in this group, there were fractures of both femurs. Six of these had fractures in or near the middle of each femur. In the seventh case, there were multiple fractures of both femurs. A patient with fractures of both femurs is counted in the table only once, a fracture of one femur being regarded as a complicating fracture of the other.

Fractures of the neck and intertrochanteric fracture of the femur occur rarely before the age of 50 but they are by far the most common types of fracture of the femur after 50. Fractures of the neck of the femur were more common in women than in men; fractures of the intertrochanteric region were distributed almost equally.

ASSOCIATED FRACTURES

In 28 (9 per cent) of the cases, a fracture of the femur was complicated by a fracture in another bone or bones. The 7 cases (2.27 per cent) in which there were fractures of both femurs are included in this group. Frequently, therefore, fracture of the femur is complicated by fracture of another bone. One should be aware of this frequency in order not to neglect an injury which might be overshadowed by the seriousness of a fracture of the femur.

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TABLE I.—SEX AND DECADE DISTRIBUTION IN ENTIRE SERIES

Decade	1	2	3	4	5	6	7	8	9	Age not stated	Total
Males	53	36	20	16	14	20	13	14	4	2	192
Females	17	5	5	6	8	12	20	33	8	1	115
Sex not stated										1	1
Total	70	41	25	22	22	32	33	47	12	4	308

TABLE II.—SEX AND DECADE DISTRIBUTION OF FRACTURES OF THE NECK OF THE FEMUR

Decade	1	2	3	4	5	6	7	8	9	Age not stated	Total
Males	0	1	0	2	0	5	4	4	0	1	18
Females	0	1	0	0	1	7	9	16	3	0	37

TABLE III.—SEX AND DECADE DISTRIBUTION OF INTERTROCHANTERIC FRACTURES

Decade	1	2	3	4	5	6	7	8	9	Age not stated	Total
Males	0	0	4	0	2	8	5	6	2	1	28
Females	0	0	0	0	2	3	5	12	5	0	27

TABLE IV.—DISTRIBUTION AS TO DECADES AND LOCATION OF FRACTURE

Decades	Separation upper epiphysis	Fracture of neck	Intertrochanteric	Subtrochanteric	Greater trochanter	Upper third	Shaft middle third	Lower third	Supracondylar	T into knee	Single condyle	Location not stated	
1				1			65	2				2	70
2	1	2		1		1	28	2	3		1	2	41
3			4	1	1	1	11	3	2	1		1	25
4		2			1	2	13	1	1	1	1		22
5		2	4	1	1	2	6	3	1		1	1	22
6		12	11	1		1	4	2	1				32
7		13	10	1		1	6		1	1			33
8		20	18				5	1		1	1	1	47
9		3	7	1			1						12
Age not stated		1	1				2						4
Total	1	55	55	7	3	8	141	14	9	4	4	7	

Although there are no examples of this in the present series, we have noticed that whenever a fracture of the femur and a fracture of the tibia occur simultaneously in the same leg, the fracture of the tibia is almost always compound.

A list of the cases in which a fracture of another bone occurred coincidentally with fracture of the femur is given in Table V.

COMPOUND FRACTURES

In the entire series, there were 11 cases (3.6 per cent) in which the fracture of the femur was compound. Table VII summarizes the cases. One case died; the mortality for compound injuries was 9 per cent.

NERVE INJURY

In only 1 case (0.3 per cent) was there injury to the nerve and this was not the result of the fracture but of the treatment. One of the attendants substituted a pillow case under the popliteal space instead of the ordinary bath towel used in the Russell method. The pillow case wadded up and produced a pressure ulcer in the external part of the popliteal space. The external popliteal nerve was involved with a resultant foot drop. This patient now shows signs of regeneration of the nerve. Nerve injury is not common in fracture of the femur, but the examination in any case is not complete without determining whether it is present.

TABLE V.—ASSOCIATED FRACTURES IN OTHER BONES

Sex	Age	Site of fracture in femur	Complicating fractures
1 M	40	Right junction middle and lower thirds	Head left fibula
2 M	32	Junction middle and lower thirds	Lower third fibula
3 M	56	Left supracondylar	Left radius and ulna
4 F	28	Junction middle and lower thirds	Right ulna
5 F	30	Left junction upper and middle thirds	Ascending rami pubis, both sides
6 F	70	Left neck	Styloid left ulna
7 M	26	Right junction upper and middle thirds	Both bones right forearm
8 M	17	Right middle third	Left humerus
9 M	48	Median condyle	Tuberosity and spine of tibia
10 F	23	Lower third	Middle of shaft of tibia and fibula
11 F	72	Left neck	Right radius
12 F	76	Junction lower and middle thirds	Skull
13 F	31	Left junction upper and middle thirds	Right tibia and fibula lower third (compound)
14 F	71	Left neck	Surgical neck left humerus
15 F	77	Right neck	Ribs
16 M	40	Junction middle and lower thirds	Left internal malleolus
17 M	60	Right middle third	Crushing injury to 3, 4, and 5 fingers left hand (amputation) and left leg (amputation)
18 M	7	Right upper and middle thirds	Right clavicle
19 M	9	Right junction middle and lower thirds	Left tibia and left radius
20 M	11	Right supracondylar	Right Colles
21 M	11	Left junction upper and middle thirds	Right clavicle

TABLE VI.—CASES IN WHICH THERE WERE FRACTURES OF BOTH FEMURS

Sex	Age		Other complicating fractures
22 F	74	Both femurs middle third	Left humerus
23 F	17	Both femurs middle third	
24 F	2	Both femurs multiple fractures	
25 M	9	Both femurs junction middle and lower thirds	
26 M	7	Both femurs middle thirds	Radius
27 M	6	Both femurs—right junction upper and middle thirds; left middle third	
28 M	8	Both femurs—left lower and middle thirds (compound); right middle third	

TABLE VII.—COMPOUND FRACTURES OF FEMUR

Sex	Age	Site of fracture in femur
1 M	50	Left lower third shaft
2 M	13	Right middle third
3 M	13	Left middle third
4 M	35	Right middle third
5 M	60	Right middle third (also had crushing injury to left leg (amputation) and three fingers left hand (amputation))
6 M	21	Right junction upper and middle thirds
7 M	80	Left middle third (died)
8 M	40	Junction middle and lower thirds
9 M	11	Left junction middle and lower thirds—also fracture right femur
10 M	11	Right femur
11 M	22	Greater trochanter (gunshot)

OPEN REDUCTIONS AND MECHANICAL FIXATION

Twenty-two (7 per cent) of the cases had some type of operative procedure performed for the fracture of the femur. Table VIII gives the list of these cases and the operative procedure.

Table VIIIA enumerates the cases of fracture of the neck of the femur which were fixed with screws by Denegre Martin's method.

Cases 13, 14, 15, 16, and 17 enumerated in Table VIII were from our wards. Only 79 (25.6 per cent) cases of fractures of the femur studied in this investigation were treated on our own service. Cases 13 and 15 were both compound fractures. Case 15 was the only instance in which Russell's method used by us in treatment of fracture of the shaft of the femur did not give a satisfactory result. (See end-results of fracture of the shaft.)

FRACTURES IN CHILDREN

Fractures of the femur in children are not uncommon. Eighty-five (27.6 per cent) of the patients were under 13 years of age. Fractures of the femur in children almost invariably occur in the middle third of the shaft. In 76 (89 per cent) of the 85 patients under 13 years of age, the fracture was in the middle third of the shaft.

Various methods were used in treating these 85 patients. Overhead traction was commonly used when the child was very young. Russell's method was also frequently employed. Reduction and immobilization in plaster and Buck's extension were also employed in some instances.

TABLE VIII.—OPEN REDUCTION AND MECHANICAL FIXATION

Sex	Age	Site of fracture	Operative procedure	Ultimate result
1 M	6	Left middle third shaft	Open reduction	Perfect result
2 M	10	Right middle third shaft	Open reduction	Unknown
3 M	12	Middle third shaft	Open reduction	On dismissal—union with shortening
4 M	2	Middle third shaft	Open reduction	Perfect
5 M	22	Shaft middle third	Former open reduction and fixation with plate. Plate removed	Unknown
6 F	60	Middle third shaft	Open reduction	Pneumonia—death
7 F	35	Middle third shaft	Fixed with Lane plate	On dismissal—angulation
8 F	20	Middle third shaft	Open reduction	Infection—malunion
9 F	30	Middle third shaft	Fixed with Lane plate	Death. Cause not stated
10 F	43	Middle third shaft	Fixed with Lane plate	Union with shortening
11 F	17	Right shaft (left femur also)	Fixed with steel plate	Alinement good but stiffness right knee
12 M	25	Lower third shaft	Fixed with Lane plate	Perfect
13 M	80	Left shaft middle third	Fixed with metal band	Died. Cause not stated
14 M	13	Epiphyseal separation head	Reduction and suspension in Russell apparatus; later wedge osteotomy	Unknown
15[1] M	21	Middle third shaft	Open reduction after failure to secure reduction by Russell's method	Unknown
16 M	52	Old fracture non-union middle third	Bone graft from tibia	Union
17 M	50	Lower third shaft	Lane plate	Union. Plate removed

[1] This case was operated upon in another hospital.

TABLE VIIIA.—DENEGRE MARTIN FIXATION OF FRACTURE OF FEMORAL NECK

Sex	Age	Site of fracture	Operative procedure	Ultimate result
18 F	76	Right neck	Fixation with 2 screws	Union—shortening; stiffness; limp
19 F	66	Right neck	Fixation with 2 screws	Slight shortening. Leg stiff at times
20 F	56	Left neck	Fixed with screws	On dismissal no union but good position with screws holding
21 F	69	Right neck	Fixed with screws	Non-union. Later head was removed and trochanter placed lower on shaft
22 M	52	Left neck	Fixed with screws	On dismissal screws in good position

The result in children is almost always good regardless of the method used. We were able to follow up 28 cases of fracture of the femur in children under 13 years of age. Twenty-three of these received a perfect result with no shortening, no weakness, no limp or residual of any kind. Of the 5 remaining, one has shortening and a limp; 3 patients report limping, but have no shortening. One of these was a patient in whom there was a fracture in each femur, one of which was compound. This patient still has a draining sinus. One patient reported a limp, weakness of the knee, and occasional stiffness with pain. Union was good without shortening.

MORTALITY

There were 22 hospital deaths, a mortality rate of 7.14 per cent. Pneumonia accounted for 10 of these deaths and possibly an eleventh. Disorientation and delirium in the aged resulted in three deaths. Fractured skull and cardiac failure in an asthenic man; uræmia, and pulmonary embolism (questionable) accounted for one death each. The cause was not determined in four instances. There were 8 cases of intertrochanteric and six cases of fracture of the neck among the 22 patients who died. This high death rate in cases with fractures of the neck and intertrochanteric region of the femur may be accounted

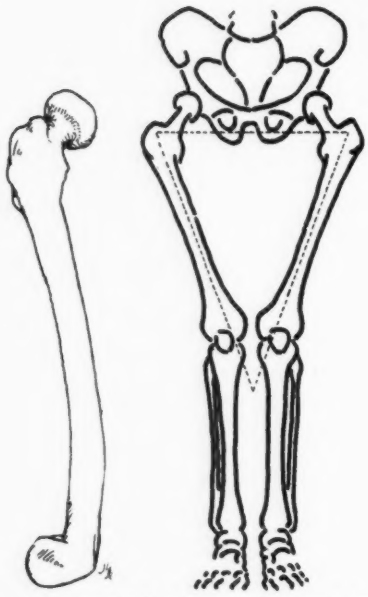

Fig. 1, left. In the lateral view the normal femur is bowed convexly forward.
Fig. 2. The triangle formed by the femurs.

for by the advanced age of the patients in this group. The mortality rate in this series for intertrochanteric fractures is 14.5 per cent and for fractures of the neck of the femur is 10.9 per cent.

ANATOMICAL CONSIDERATION

In viewing the femur from the standpoint of normal contour, one is impressed with several striking points in its conformity. In the lateral view, it is obvious that the normal femur is bowed convexly forward (Fig. 1). It is important to preserve this bow because if it is decreased or increased, it will result in the weight bearing line of force falling either posterior or anterior to its normal position in the foot. Viewing the femur anteroposteriorly, the shaft again is bowed slightly with the concavity inward. When the individual is standing erect or lying supine with the heels together, the shaft of the femur passes downward and inward from the greater trochanter and each femur may be regarded as part of a side of an isosceles triangle whose base is formed by an imaginary line between the trochanters and whose apex is at the intersection of lines projected below the knee in the direction of the shaft of the femur (Fig. 2). The neck of the femur usually joins the shaft at an angle of about 125 degrees. Decrease in the angle results in a varus deformity with the effect of shortening of the femur and tilting of the pelvis toward the affected side to compensate for the deformity.

Whatsoever may be said for the contention that the ultimate end in the treatment of fractures is perfect functional result, the proximal aim in the treatment must be directed toward attaining a perfect anatomical result and by this, a perfect functional result may be obtained. In fractures of the femur as in other bones of the body, it is most desirable to have perfect apposition of fragments without angulation or shortening. By careful attention to detail and repeated checks on the alinement, we have found that this can be obtained very often indeed.

Muscles play a very important part in position of fragments in fractures of the femur; gravity a no less important rôle. These two forces must be satisfied to obtain and maintain correct apposition and alinement of fragments. The usual displacement varies considerably, depending on the level of the fracture. The displacement at different levels is more or less characteristic, in fact, almost constant, with the necessary exceptions to justify the generality. When such is the case, it is due to more constant forces such as gravity and muscle tone and not to the extreme variable—the direction of the fracturing force.

When the fracture is in the neck of the femur, the upper fragment is still attached by the ligamentum teres and the vacuum force of the acetabulum. The muscles running from the pelvis to the leg exert a shortening action while the external rotators with the force of gravity combine to carry the trochanter back and externally rotate the shaft. The same forces act in a similar manner on the lower fragment when there is an unimpacted intertrochanteric fracture. Here, the capsule of the joint may also assist in holding the upper fragment in position.

If the fracture detaches the lesser trochanter, this fragment may be displaced upward and forward by the iliopsoas. If the greater trochanter is broken off, the gluteus medius and minimus, pyriformis, gemelli, and obturator internus tend to displace it upward and backward.

In a pertrochanteric fracture, one passing transversely across the shaft between the two trochanters, the upper fragment is abducted and externally rotated while in a subtrochanteric fracture, the additional action of the iliopsoas on the upper fragment tends further to rotate it externally and flex it. In fractures in this region as in fractures at other levels across the bone upward displacement of the lower fragment is prone to

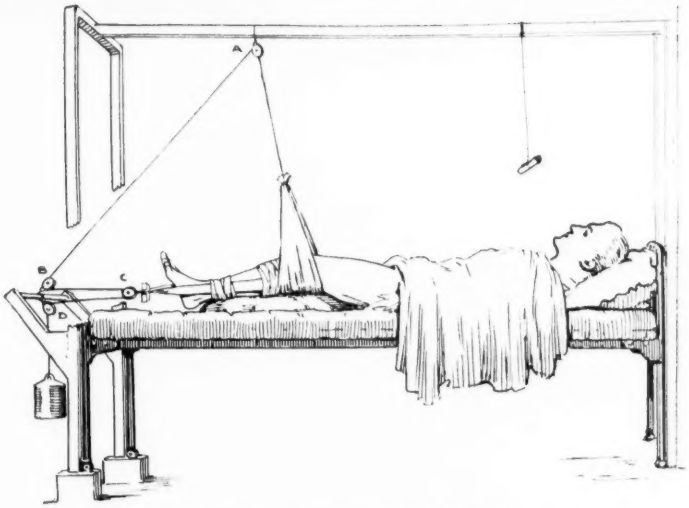

Fig. 3. Russell's method (From Russell, Brit. J. Surg., 1924, ii, 491).

occur due to the action of the muscles bridging the line of fracture. In securing alinement in pertrochanteric and subtrochanteric fractures and fractures of the upper part of the upper third of the femur, we believe that the lower fragment must be brought in line with the prereduction position of the upper fragment, i.e., into abduction, whereas we do not believe that the lower fragment should be brought in the line of the prereduction position of the upper fragment, if it is abducted, in fractures in the lower part of the upper third, the middle third, or the upper part of the lower third of the shaft as we shall show.

In fractures of the shaft, the lower fragment is almost constantly displaced posteriorly and upward with relation to the upper fragment and this is partially due to the action of gravity, partially to the tone of the gastrocnemius and popliteus and plantaris muscles flexing the lower fragment on the leg while the muscles bridging the site of fracture produce shortening. Moreover, the adductor muscles are of the greatest importance in fractures of the shaft. The strong adductors tend to displace the fragments inward and they exert a more decided effect on the lower fragment since in the upper fragment, adduction is opposed by the attached abductors. The adductor longus pulling up on the adductor tubercle tends to shorten the distance between the inner condyle and the pubic ramus. Abductors tend to abduct the upper fragment and thus an angulation with the convexity outward is often produced, especially when the fracture is in the middle of the shaft. To overcome this angulation and to secure sagittal alinement, it is practically and even theoretically incorrect to carry the lower fragment into the prereduction line of the upper fragment, i.e., abduction. On the contrary, the leg and lower fragment must be carried into adduction to relax the muscles which are producing the deformity. In a number of cases we have proved this repeatedly to our satisfaction that to correct external angulation of the femur in fractures of the shaft, the leg must be carried into adduction. Abduction only increases deformity. This sagittal alinement is easy to correct and maintain; it is only shortening and posterior displacement of lower fragment which offer any difficulty.

In supracondylar fractures, the lower fragment is flexed on the lower leg and upwardly displaced. Here gravity again and the gastrocnemius, popliteus, and plantaris each play a part in producing the posterior displacement. Muscles bridging the fracture effect the shortening. T or Y fractures into the knee joint are in effect supracondylar fractures but with the added complication of involvement of the joint and sometimes of separation of the condyles.

Fractures of single condyles may or may not be attended with displacement. Here muscles play less a rôle and the resulting displacement is largely the result of the fracturing force.

In epiphyseal separation at the lower epiphysis of the femur, the lower fragment is generally

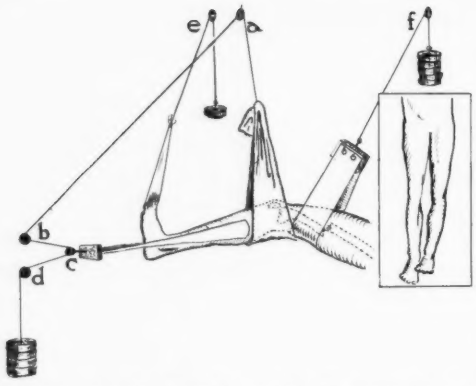

Fig. 4. Modified Russell's method. The upper band is added to correct posterior displacement of the lower fragment.

anteriorly displaced and is flexed on the lower leg. Why the anterior displacement occurs is hard to explain, but so frequently was this lesion produced by a particular force, e.g., a boy getting his leg caught in the spokes of a wagon, that it became known as a cart wheel fracture and in absence of a better explanation, the fairly constant displacement may be attributed to the particular fracturing force.

METHODS OF TREATMENT

In this series various methods of treatment have been used. In the other fracture services of Charity Hospital, the routine differs from the methods used in our wards. We shall, however, outline only the routine and the methods used in our service. Seventy-nine of the 308 cases reported in this article were treated in our wards. Anatomically, these 79 fractures were divided as itemized in Table IX.

Modification of Russell's method in treating fractures of the shaft of the femur. In 1924, Russell, of Melbourne, described his method of treating fractures of the femur. We believe that this is the method of choice in treating fractures of the upper, middle, and lower thirds of the shaft of the femur above the supracondylar region and below the subtrochanteric region. The method is intended to rest the muscles in their most accustomed position and by a combined pull on the knee and the lower leg to exert a force on the lower fragment of the femur in the normal line of the shaft (Fig. 3). A bath towel is placed under the popliteal space. To suspend the leg at the knee by this towel, a rope passes up and around a pulley *A*, from which pulley a perpendicular dropped

TABLE IX.—ANATOMICAL CLASSIFICATION

	Cases
Epiphyseal separation head	7
Neck fractures	1
Intertrochanteric fractures	2
Greater trochanter	
Subtrochanteric	
Shaft	
Supracondylar	
Supracondylar T	
Not classified	
	1

would fall just below the tubercle of the tibia. Thence the rope passes around pulley *B* on the foot of the bed and back and around pulley *C* which is attached to a spreader separating lateral strips of adhesive applied to the sides of the lower leg. Then the rope passes back and around pulley *D* which is just below pulley *B* on the foot of the bed. A weight of 8 pounds (for adults) is fastened to the end of the rope. Russell emphasized the necessity of putting the leg into a position which is most natural for the muscles. He recommended the use of a pillow under the knee and the thigh to counteract posterior displacement of the lower fragment.

The only difficulty encountered was the tendency to persistent displacement of the lower fragment and one of us[1] instituted the use of the upper band shown in Figure 4 to overcome this. This band is made of canvas and is separated from the skin of the thigh by cotton. It is suspended on either end by hooks on a 1 by 1 inch piece of wood the length of which is the width of the canvas. From the center of this strip of wood, a rope passes up and cephalad around a pulley and 10 pounds of weight are placed on the end of the rope. This last pulley should be placed so that the pull is perpendicular to the thigh.

We use Blake's footstrap to prevent foot drop. As far as rotation is concerned, it is hardly necessary, for, as Russell has said, the towel under the popliteal space prevents this undesirable displacement.

To secure alinement in the anteroposterior view when the fracture is in the middle or lower third of the shaft, the leg is carried into adduction across the midline. This invariably has the desired effect and one should not be beguiled, when the upper fragment is in more abduction than the lower, into attempting to bring the fragments into alignment by further abducting the lower leg. It seems paradoxical but correction here is obtained by bringing the lower fragment away from the line of the upper, i.e., to adduct the whole leg. This re-

[1] Muir Bradburn.

lapses the adductor muscles, which produce the deformity. When the fracture is in the upper part of the upper third of the shaft, i.e., almost in the subtrochanteric region, the leg must be abducted. Here the abductors have control of the upper fragment and the lower fragment must be brought into the prereduction line of the upper fragment.

It is desirable to institute immediate treatment in fractures of the femur. Examination should be done at once, an X-ray should be taken immediately, and when the nature of the injury has been ascertained to be a fracture of the shaft of the femur and Russell's is the method selected for treating, the leg should immediately be suspended in the apparatus. Morphine may be given but an anæsthetic is not necessary. We have found that when delay is encountered some difficulty may be had in overcoming shortening and displacement. Shock does not contra-indicate the application of the apparatus. Occasionally, we have found it necessary to use more than 10 pounds on the lower "hook-up" for a few days, especially if the individual is very obese or very muscular. This weight must be reduced after correct position is obtained; otherwise, overextension may result and persistent overextension is to be avoided.

Repeated X-ray examinations are necessary, especially during the time perfect alinement is being secured. At the end of 4 days, the fragments should be in perfect alinement but this sometimes means several adjustments of the apparatus to secure changes in position.

We keep our adult patients in this form of traction about 8 weeks; adolescents about 6 weeks. Toward the latter part of this period, the patient is measured for a Thomas walking caliper brace, which is applied immediately when the traction is removed. The patients wear the brace day and night for 1 month; they take it off at night but continue to wear it when walking until from 5 to 6 months have elapsed from the time of the injury. They should remove the shoe daily, wash the foot, and put on a clean pair of socks. They are instructed to keep the knee hinge locked when they are walking and to open it each time they sit down. Moreover, they are instructed to sit on a table each day and work their leg with a muscle exerciser attached in order to mobilize the knee (Fig. 5).

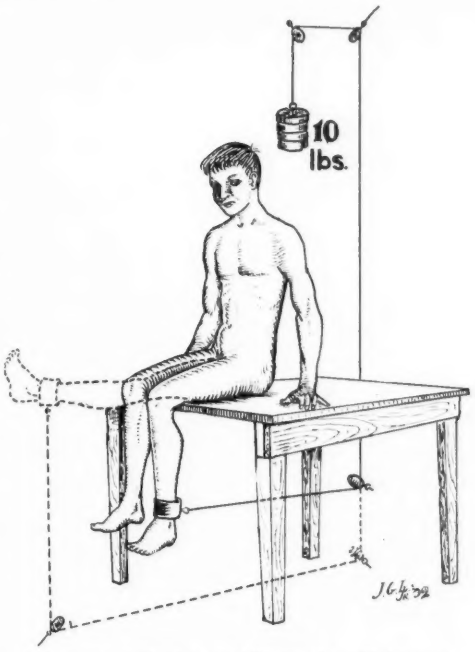

Fig. 5. A method of mobilizing the stiff knee after fracture of the femur. The dotted outline represents stiffness in extension.

Fractures of the shaft. The technique we use has secured excellent results in our hands. In this series, there were 31 cases of fracture of the upper, middle, or lower thirds of the shaft of the femur admitted to our service. One was a compound fracture on which an open reduction was done and the fragments were fixed with a Lane plate. Subsequently the plate had to be removed. The end-result is not known. One was an old fracture of the shaft with non-union. A bone graft was done and union resulted. Three of the patients transferred to other hospitals and were thus not treated entirely by us. One of these patients was treated by Russell's method in the other hospital. The result was unsatisfactory and an open operation was done. One patient, 80 years of age, had a compound fracture and an open operation was done immediately. This patient died. The 25 remaining were treated by the modified Russell method described herein. Two died. One, a patient 68 years old, developed diarrhœa and delirium and died and one aged 71 years died from a cause recorded as bronchitis. In none of the remaining 23 cases was it necessary to do an open operation. We have been able to follow up 9 of the 23; 7 of the 9 obtained a perfect result with no limp, no shortening, no stiffness, and no weakness. Another wrote that he had a perfect result with no shortening, no stiffness, but he also stated that the muscles of the affected leg were a little weaker than of the other leg. He attributed this to disuse and said the strength of the limb

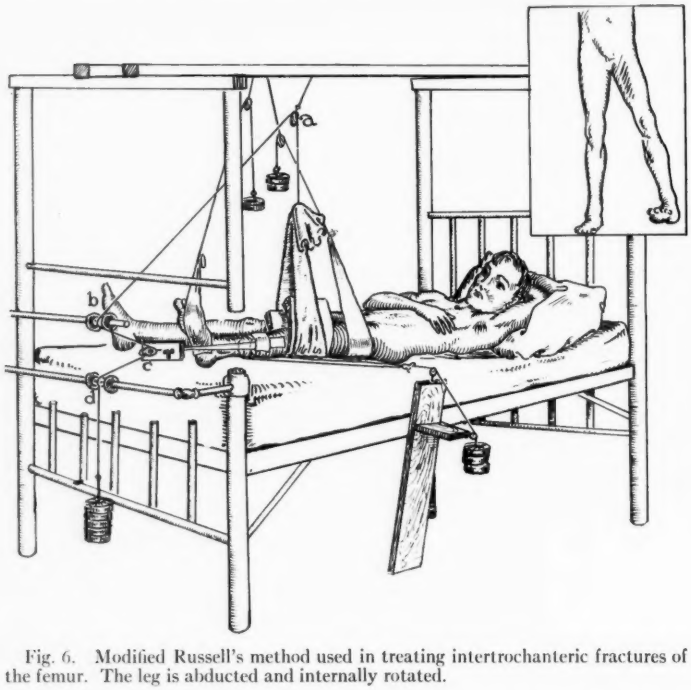

Fig. 6. Modified Russell's method used in treating intertrochanteric fractures of the femur. The leg is abducted and internally rotated.

was improving. The ninth patient replied that his result was not exactly perfect, that his leg was strong and he did not limp, but that he had some stiffness of the knee and the affected limb was about one inch shorter than normal. An X-ray picture taken before dismissal from the hospital showed good position with callus.

Fractures of the neck of the femur. Whitman's method has probably given the highest percentage of good results in the treatment of fractures of the neck of the femur. We have used a method modified from Russell's traction in the treatment of these fractures. So far we have not employed it in a sufficient number of cases to report on its efficiency.[1] The application of the Russell apparatus in treating fractures of the neck of the femur makes the patient far more comfortable than if he is encumbered with a cast. The apparatus is applied in the usual manner but the leg is carried into marked abduction by swinging the lower pulleys out (Fig. 6). The leg also is rotated internally by an adhesive band which is started on the lateral aspect of the leg and runs up and in and around the leg. It is faced with another piece of adhesive where it comes in contact with the posterior aspect of the limb and from this adhesive a rope passes out and around a pulley. Six pounds are attached to the end of the rope. It is essential to attend diligently to the adhesive straps and replace them with fresh ones at the first signs of slipping.

In the elderly individual, we screw the fragments together with two wood screws after the method described by Denegre Martin. The necessity of getting the elderly patient out of bed is paramount. Approximating the fragments with wood screws is a relatively simple operative procedure and may be done under local analgesia with little discomfort to the patient. The operation does not expose the fracture or open the joint. Two drill holes are made in the external surface of the femur just beneath the greater trochanter. The drills, just a little larger than the unthreaded shank of the wood screw, are directed toward the head through the medullary portion of the neck of the femur. They only drill through the cortex. The screws may be pushed up to the head of the femur without resistance. They grip the detached head and with free rotation of the unthreaded

[1] Since this paper was submitted for publication we have used this method in 4 cases and non-union resulted in each instance. From our experience we would condemn the method in the treatment of fractures of the neck of the femur.

portions of the shank in the drill hole, the screws approximate the head to the distal fragment (Fig. 7). If the patient is not too sick, we perform the operation within 24 hours after admission. We have used this method recently in middle aged individuals with excellent results. They are permitted out of bed in 3 to 5 days but are not allowed unsupported weight bearing on the affected limb until union is complete.

Intertrochanteric fractures of the femur. Intertrochanteric fractures are closely related to fractures of the neck of the femur. The prognosis as regards union is better in intertrochanteric than in fractures of the neck of the femur. Intertrochanteric fractures are extracapsular which makes a decided difference due in great part we believe to the fact that the fracture line is not bathed with synovial fluid. Synovial fluid seems to interfere with union—a factor which we are attempting to prove experimentally in dogs.

In intertrochanteric fractures, we use the same methods given for fracture of the neck of the femur. We have had enough experience to say that Russell's apparatus yields excellent results (Figs. 8 and 9), and at the same time keeps the patient comfortable. The leg must be abducted and internally rotated. Martin's method is also of decided value in the treatment of intertrochanteric fractures and as many of these patients are old, we sometimes use it.

Pertrochanteric fractures of the femur. In the pertrochanteric fracture of the femur, the upper fragment is generally markedly abducted and externally rotated. Russell's method is applicable in the treatment but the lower fragment must be brought in line with the upper, and, therefore, the limb is carried into abduction and is externally rotated by lateral skin traction applied in a manner analogous but in an opposite direction to that used in securing internal rotation, in fractures of the neck of the femur.

Subtrochanteric fractures. In addition to being abducted and externally rotated, as in pertrochanteric fractures, the upper fragment in a subtrochanteric fracture is under the additional influence of the iliopsoas muscle and may be markedly flexed. Russell's apparatus is still applicable in these cases but the pulleys at the foot of the bed should be elevated to produce flexion of the hip. In treating this fracture, however, we prefer to use a Steinmann pin, Kirschner wire, or calipers at the lower end of the femur to obtain skeletal traction.

Fractures of the greater and lesser trochanters. When the greater trochanter is fractured, there may or may not be displacement. If displacement is not present, it is sufficient to put the patient at rest, immobilizing the leg for 6 weeks. Suspended traction is much more comfortable and just as efficient as immobilization in a cast. When separation is present, it is generally characterized by upward and backward displacement of the trochanter and the limb is put in a position of abduction, external rotation, and flexion at the hip. Here again, we prefer suspended traction with the Russell apparatus to immobilization in a cast.

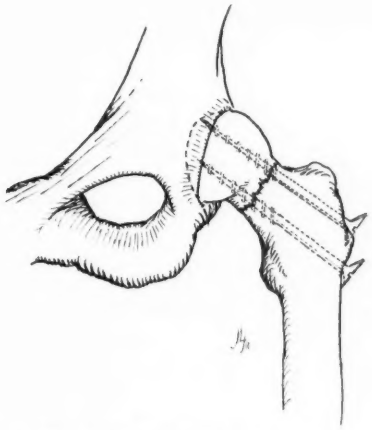

Fig. 7. The use of wood screws to approximate and fix the fragments in fracture of the neck of the femur. Denegre Martin's method.

When the lesser trochanter is fractured, it may or may not be separated from the shaft. If separation is not present, immobilization for a period of time sufficient to permit union is all that is necessary. When separation is present, it is characterized by forward and upward displacement of the trochanter by the iliopsoas. Approximation of the fragments can be best secured by flexing and externally rotating the thigh and the limb is immobilized in this position by skeletal traction or by a plaster spica extending from the nipple line to and including the foot.

Epiphyseal separations of the femur. Separation of the epiphyses is fortunately rare. When separation of the upper epiphysis occurs, it is in immediate effect comparable to the fracture of the neck of the femur. However, the remote effects differ because of the age of the patient. It is essential to secure exact reduction. This is attempted under anæsthesia and if successful, the limb is maintained in abduction and internal rotation by the use of Russell's apparatus applied in the manner described for fractures of the neck

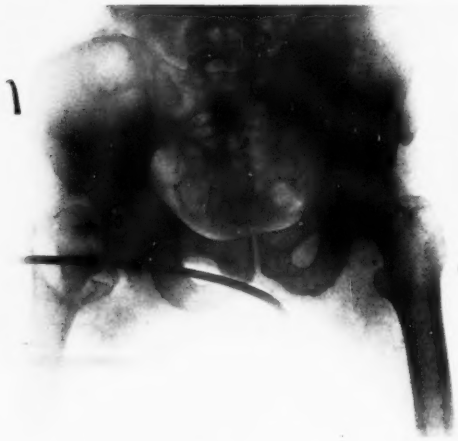

Fig. 8. Intertrochanteric fracture on admission in Thomas splint.

Fig. 9. Union intertrochanteric fracture in good position. Same case as shown in Figure 8 after treatment by modified Russell's method (Fig. 6).

of the femur. The apparatus is removed after 6 weeks. The youth is allowed to bear weight unsupported after 6 to 8 weeks. Open reduction is to be resorted to if success is not achieved by the closed method. Replacement of the conical upper end of the diaphysis in the concavity of the upper epiphysis is the end in view. Excision of the upper epiphysis is reserved for long standing cases in which traumatic arthritis has developed and a satisfactory functional result otherwise seems impossible.

When the lower epiphysis is separated from the shaft, immediate reduction under anæsthesia should be accomplished. The limb is immobilized in a plaster cast in the position of flexion at the knee. After 2 weeks, the cast is bivalved and daily gentle motion is begun. After 6 weeks, the patient may be permitted supported weight bearing.

Supracondylar fractures of the femur. We have used Russell's apparatus in treatment of supracondylar fractures of the femur and have found the method unsatisfactory in these fractures. Here there is marked posterior displacement of the short lower fragment. It is flexed on the lower leg. Russell's apparatus does not permit the degree of flexion of the knee necessary in these cases to secure proper alinement of the fragments. Too frequently, posterior displacement of the lower fragment persisted when we used Russell's method. Therefore, we have discarded this method and are using skeletal traction with satisfactory results. The method is shown in diagram in Figure 10. Traction is obtained by passing a Steinmann pin through the tibia just posterior to the crest and just below the tubercle. A well padded double inclined plane is placed under the leg with an obtuse apex angle of about 115 degrees. The boards are so arranged that the apex presses up on the lower fragment. From the horseshoe attached to the Steinmann pin in the crest of the tibia, a rope passes down and over a pulley on the foot of the bed. This pulley must be at such an elevation that it is below the level of a line projected from the shaft of the femur. In other words, the pull is so directed that the posteriorly displaced lower fragment is pressed up by the apex of the double inclined plane. In adults, 25 pounds for 36 to 48 hours are necessary to secure reduction; then the weight is reduced to 15 pounds to maintain the position. The patient is maintained in this apparatus until mild union is obtained (5 to 6 weeks) and then Russell's apparatus is substituted and the patient remains in suspended traction for an additional 3 or 4 weeks. The after-treatment is similar to that used in fractures of the shaft of the femur.

Y fractures of the lower end of the femur into the knee joint. Y fractures of the lower end of the femur into the knee joint are closely allied to supracondylar fractures of the femur. If there is marked separation of the condyles, we attempt to overcome this by use of the Boehler screw clamp. If this is not successful, a wood screw is used to approximate the fragments. The injury is then treated as a supracondylar fracture. If the frac-

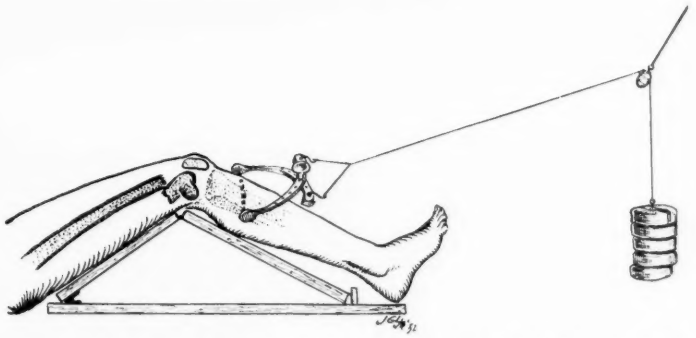

Fig. 10. Method used in treating supracondylar fracture of the femur. The line of traction is below a line projected from the femur and the apex of the doubly inclined plane presses up on the lower fragment.

ture is complicated by hæmorrhage into the knee, the bloody fluid is aspirated and the joint is lavaged with normal saline. This is repeated as often as is deemed necessary.

Fracture of a single condyle. In fractures of the condyles there is no displacement of the fragments, fixation in a plaster cast is an adequate method of treatment. Here synovial fluid, we believe, is prone to delay union and no non-supported weight bearing is permitted for 4 to 6 months. When there is displacement of the fragments, reduction may be accomplished by manipulation of the fragments when the patient is under anæsthesia but if this is not successful, longitudinal traction on the leg with lateral bands to correct varus or valgus or open reduction and fixation with a wood screw is resorted to.

END-RESULTS

It is to be remembered in reading these results that the patients were treated by many different men using a variety of methods.

It was very difficult for us to follow the class of patients reported in this paper. They are the poorest people of the city and state, not infrequently uneducated, frequently unintelligent, and often they change their addresses. Consequently, as would be expected, the percentage of those we were able to follow to determine the end-results is low. We sent out questionnaires to all those patients who were dismissed from the hospital. We asked if they had a perfect result or if they had limp, weakness, stiffness, shortening, union or non-union, and also how long it took them to get over the disability resulting from the fracture. We received but 84 replies. Twenty-eight of these were from patients who were under 13 years of age at the time they were admitted to the hospital. As already stated the middle of the shaft was the part usually affected in children. Twenty-three (82 per cent) of the 28 replies received from the children showed that the child had a perfect result with no residual of any kind whatsoever. The 5 remaining were partially disabled. It is remarkable what powers of repair and compensation are ready in youth to overcome the injury. One of these children had union with overlapping and shortening of a centimeter to a centimeter and a half at the time of dismissal and now has a perfect result with no residual of any kind. In the growing child, the shortened bone may grow faster than that of the opposite leg so that the asymmetry is overcome.

From patients over 12 years of age at the time of the injury, we received 56 replies. These are tabulated in Table X. In computing the results, we considered as totally disabled those patients who were confined to bed or who had still to use a brace or crutches or both; as partially disabled, patients who could walk but who had some residual, limp, stiffness, shortening, weakness, etc.; and as perfect results, only those patients who had absolutely no remaining evidence of the former fracture.

Supracondylar fractures and subtrochanteric fractures show the greatest percentage of imperfect results. Replies from 4 patients with supracondylar fractures and one with supracondylar T fracture show that 2 of the 5 are totally disabled, 2 are partially disabled, and only 1 had a perfect result.

Both of the 2 patients with subtrochanteric fractures who replied had imperfect results with limp and shortening.

Only 3 (23 per cent) of 13 patients with fractures of the neck of the femur had a perfect result.

TABLE X.—RESULTS OF FRACTURES OF THE FEMUR IN PATIENTS OVER TWELVE YEARS OF AGE

Location of fracture	Replies	Perfect results	Imperfect results	Totally disabled	Bedfast	Partially disabled	Patients not bedfast					
							Patients having limp	Patients having weakness	Patients having stiffness	Patients having non-union	Patients having shortening	N... pa... y
Neck of femur	13	3	10	4		6	10	9	8	4	8	
Intertrochanteric	14	4	10	1	1	8	6	4	5	3	7	
Subtrochanteric	2		2				2				2	
Upper third shaft	1	1										
Middle third shaft	19	11	8			8	6	1	6		1	
Lower third shaft	1	1										
Supracondylar	4	1	3	1		2	2	2	2		3	
Supracondylar T	1		1	1			1	1	1			
Single condyle												
Epiphyseal separation												
Unknown	1	1										
Total	56	22	34	7	1	24	27	17	22	7	21	

Five (38 per cent) are totally disabled, and 5 (38 per cent) are partially disabled. Four (30.7 per cent) report non-union. One patient with fracture of the neck of the femur died after leaving the hospital. This case is not included in the computations of end-results.

Intertrochanteric fractures show a higher percentage of good results. Four (28.6 per cent) of 14 patients had a perfect result. Two (14 per cent) are totally disabled. Eight (57 per cent) are partially disabled.

Twenty-one patients with fractures of the shaft of the femur responded. One of these had a fracture in the upper third, one had a fracture in the lower third of the shaft. Both of these patients had a perfect result. The remaining 19 had fractures in the middle third of the shaft of the femur. Of these 21 patients, 13 (62 per cent) had perfect results, none is totally disabled, 8 (38 per cent) are partially disabled.

SUMMARY

Three hundred and eight cases of fracture of the femur received treatment in the wards of Charity Hospital, New Orleans, from June 1, 1929, to May 31, 1931. One hundred and ninety-two of the patients were males, 115 were females (1.67:1), and the sex could not be determined from the record of one. Seventy-nine of the patients were on the author's service.

The first decade of life was the decade most often affected, there being 70 cases in our series. Thirty-six per cent of the patients were under 20; 41.88 per cent were 50 years or older.

The shaft of the femur, especially of the middle third, is the most common site of fracture in the first and second decades of life; the intertrochanteric portion and the neck are the sites more commonly affected after 50 years of age.

Although there were fewer females than males in the entire series, there were proportionately more women than men with fracture of the neck of the femur and with intertrochanteric fractures.

Nine per cent of the cases were complicated by fractures in other bones. Two and twenty-seven hundreds per cent of the cases had fractures in both femurs.

In 3.6 per cent of the cases the fracture of the femur was compound.

Nerve injury was uncommon. It occurred once but was the result of the treatment instead of the fracture.

Fracture of the femur in children occurs almost always in the middle third of the shaft. The results were almost always excellent, in spite of a variety of methods used.

In 22 of the 308 cases of fracture of the femur, some sort of operative procedure was done.

The mortality rate for the 308 cases was 7.14 per cent; for intertrochanteric fracture alone, 14.5 per cent; and for fractures of the neck of the femur, 10.9 per cent.

The methods we prefer are briefly described. In treating fractures of the shaft of the femur Russell's method with slight additions is our choice. In treating fractures of the intertrochanteric region, we also use a modification of Russell's method.

Eighty-four replies were received from the questionnaires sent to the patients. Twenty-eight replies were from children under 13 years of age at the time of their admission to the hospital; 23, or 82 per cent, of these received perfect results. Fifty-six replies were received from patients over 12 years of age at the time of their admission to the hospital. Those with fractures of the shaft of the femur show the best results (62 per cent perfect). Patients having fracture of the neck of the femur showed 23 per cent perfect results; 38 per cent are totally disabled, and 38 per cent are partially disabled. Thirty and seven-tenths per cent have non-union. Twenty-eight per cent of 14 patients with intertrochanteric fractures had perfect results. Fifty-seven per cent are partially disabled and 14 per cent are totally disabled. Eighty per cent of 5 patients with supracondylar fractures have persistent disability.

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RENAL COMPLICATIONS OF BILIARY TRACT INFECTIONS

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IN 1928 the occurrence of acute nephritis with suppression of urine as a complication of severe biliary infection was forcibly called to our attention (Case 1). Since that time we have customarily estimated all cases of gall-bladder disease from the standpoint of renal function. Meanwhile we have seen renal failure in 5 more patients (Cases 2, 3, 4, 6, 12) and have found a similar case history (Case 5) in our records of less recent date. The occurrence of so grave a renal complication in 6 of these 7 cases of a total of 56 patients with disease of the biliary tract under the care of my father and myself since Case 1 is certainly not a common experience in the practice of most surgeons. It is an indication of the fact that we, at least, have to deal with very sick individuals, particularly during times of economic stress. The fact is that singularly few clinicians have concerned themselves with the possibility of renal failure in biliary infections, whereas the chances for permanent damage to the liver, pancreas, and heart are fairly generally appreciated. Judd reported before the Section on General Surgery of the American Medical Association in 1932 an incidence of circulatory system disease over 50 per cent higher among patients with surgical diseases of the biliary tract than was the incidence for the age group according to the statistics of life insurance companies.

The majority of the few cases reported has been in the German literature. Clairmont and Haberer in 1911 presented 5 cases of renal failure occurring after operations on the biliary system; 2 patients recovered. The presentation of the individual cases is so incomplete that a critical evaluation of them is difficult. Preoperative urine findings were normal in 1 case and were indicative of kidney damage in another. The occurrence of jaundice was constant, but postoperative bile drainage is mentioned only once. All patients but one were subjected to cholecystectomy and choledochostomy under chloroform anæsthesia. No indication is given of the competency of the circulation to maintain output of urine, and it seems probable that in only 1 of the 3 fatal cases was suppression of urine due to nephritis. These authors did not succeed in producing anuria experimentally by ligation of the common duct in dogs though renal function by dye excretion sometimes showed impairment. They concluded that the dog was not a useful experimental animal for the purpose, that anuria was always the result of parenchymatous damage in clinical cases of deep jaundice, and that surgeons might have to content themselves with cholecystostomy in such patients. In the same year Steinthal mentioned having seen such a case in which anuria developed on the fourth day after operation with death and characteristic autopsy findings of acute tubular degeneration. He considered that the anæsthetic had been the precipitating factor, there having been a latent renal insufficiency as a sequela of liver damage. Beck and Simon also reported having seen such cases die in uræmia without operation. Staeheli, in 1921, presented a case of his own, the patient dying anuric 3 days after cholecystectomy and choledochostomy; there had been albumin in the urine before operation; autopsy showed petechial hæmorrhages into all the organs. He reviewed 3 of the cases of Clairmont and Haberer and a case of Kehr's, that of a 65 year old man, jaundiced, who put out only 200 cubic centimeters of urine before death 4 days after cholecystectomy; autopsy in this case showed only jaundice of all organs and arteriosclerotic kidneys. Staeheli believed anuria to be the sum of many factors, most prominent of which are long duration of disease, infection, and deep jaundice. As for the effects of anæsthetics, acute yellow atrophy of the liver was not found at autopsy in any of the cases reviewed and tubular necrosis (attributable to ether) in only one. In common with the previously quoted authors, he postulated a primary liver failure to detoxify substances which then damage the kidneys. He recommended careful functional tests of the kidneys before operation and urged early operation in acute severe cholecystitis to avoid renal complications. With the latter recommendation, we must heartily disagree not simply for the reasons ordinarily urged, but because of evidence on this particular problem to be presented later. Abrahamson reported studies of renal function in 15 cases of jaundice due to various causes. None of his cases showed evidence of renal insufficiency (retention of nitrogen, salt, or water) and he felt that there was no significant change in the ability of his patients to excrete phenolsulphonephthalein. However, he has included as normal one case in which

phenolsulphonephthalein excretion was 35 per cent, 2 in which it was 40 per cent, one of 45 per cent (all in 2 hours after intramuscular injection), and one in which it was 40 per cent 2 hours after intravenous injection. Two of these patients had albumin and hyaline and granular casts in the urine. We do not consider these normal figures for phenolsulphonephthalein excretion in patients ranging from 23 to 50 years of age. It is our opinion that only 6 of his 15 patients showed really satisfactory dye excretion (60 per cent after intramuscular injection in 2; 60 per cent in 1, and 65 per cent in 3 after intravenous injection). Abrahamson urged quite properly that if dye excretion were low, extensive operation was to be guarded against, whereas a normal dye excretion offered some assurance that postoperative renal failure was unlikely to occur. With certain exceptions, to be discussed later, we quite agree to these proposals.

Wilensky and Colp made observations on the nitrogen partition of the blood in a large series of patients with biliary tract disease, before and after operation in many cases; some of these patients had evidence of nephritis, though it is not made clear that any of them developed suppression of urine. The many observations in their last two papers are valuable material from which to draw conclusions, though the conclusions to which we have come from a study of their figures differ widely from those of the authors. It is necessary to be specific in the discussion of these papers.

In the second paper, Table I lists 56 cases of biliary tract diseases without jaundice or other complication and with normal blood nitrogen figures in all. Table II contains 13 "mild and moderate cases with jaundice but without demonstrable kidney involvement or other complication." Four cases have blood non-protein nitrogen values of 50 (2 cases), 62.9, and 71.7. The authors consider all of these as being within normal limits, apparently, explaining the 2 last figures as being probably due to excessive nitrogenous intake in diet, and conclude that varying degrees of jaundice "in the absence of kidney complications apparently do not influence . . . . the blood figures for . . . . non-protein nitrogen." Table III comprises 8 cases of mild and moderate biliary tract disease with or without mildest albuminuria and a minimal number of casts. Only one of these patients was jaundiced; they are commented on as having no nitrogen change although 3 cases had non-protein nitrogen values of 49, 57.7, and 60! Table IV lists the findings in 9 cases with proved structural liver changes and it is the authors' comment that no particular change in blood nitrogen is noted; in the 2 patients who died, however, non-protein nitrogen was 60 in one and uric acid was 5.3 in the other (non-protein nitrogen not determined). That the objections raised to the authors' deductions from pre-operative observations in the foregoing tables are valid is also borne out by the later behavior of the 8 patients (Cases 39, 49, 52, 75, 80, 81, 82, 83) in question when one follows them in Tables V and VI of the second paper and in Table III of the third paper. In Cases 30, 52, and 83 apparently no operation was done; Case 49 has no postoperative determinations recorded; Cases 75, 80, 81, and 82, patients died after operation, the first with a falling, the third with a rising non-protein nitrogen, and no postoperative determinations on the others. The 4 postoperative deaths among these 5 patients operated on occurred in patients who were not jaundiced, 3 of them being in acute attacks of gall-stone disease and the fourth just after an acute exacerbation. Further figures of value are given in Table V of the second paper which deals with comparisons of pre-operative and postoperative blood nitrogen. A large increase occurred in 18 per cent of the cases; reference to previous tables shows that this occurred, with one exception, in cases operated on during an acute attack. The author reports 18 per cent of cases showing a decrease following operation (Cases 3, 54, 58, 75, 77), but in the first 3 cases the difference ranges from 0.8 to 2.4 milligrams per 100 cubic centimeters, approximating the limits of error of the method; Case 75, patient died although the non-protein nitrogen fell from 60 to 40; Case 77, patient's pre-operative non-protein nitrogen was 44.4, is variously listed as having a postoperative value of 33.3 in Table V and of 66.5 in Table XVI where it appears with the cases classified as having both jaundice and nephritis.

There is, in general, much difficulty in reconciling the authors' comments in their text with the figures that appear in their tables. It is obvious that they have not recognized that retention of nitrogen occurs in some acute exacerbations of cholecystitis, whether previous attacks have occurred or not, in the absence of jaundice and perhaps with normal urine. Their clinical observations, however, have impressed them with the importance of jaundice in causing renal lesions subsequent to hepatic cell damage and with the further effect of anæsthetics, notably ether, on an organism that is, perhaps, barely compensated previous to operation. We must disagree sharply with their observation that the simplicity or severity of the operation itself is of little consequence. Any important lowering of the alkaline reserve as a result of anæsthesia or operative trauma should seriously threaten a precarious liver and kidney function. The fact that of the 18 cases these authors classify as having been severely sick, the 6 postoperative deaths and the 2 non-operative deaths occurred in acute cases should be ample indication of how poorly acutely sick patients withstand an added surgical insult.

Walters and Parham reported 2 patients dying of renal insufficiency, one before, the other after, operations for the relief of jaundice. They made the observation that following ether anæsthesia the blood nitrogen sometimes doubled in amount on the second and third postoperative days. They differentiated clearly between hepatic and renal insufficiency in these complicated cases

". . . . associated with the former there is abundant drainage of light colored bile containing small amounts of the bile pigments . . . . little change occurs in content or volume of the urine, and the blood urea remains persistently low."

It is not our purpose to go into the extensive literature on jaundice, but a few outstanding facts pertinent to this discussion deserve mention. Rowntree, Snell, and Greene have made experimental investigations on obstructive jaundice in the most exhaustive detail. In the dog they did not observe suppression of urine and they found the blood nitrogen and its partition largely unchanged except for a terminal rise; uric acid did not appear. Bile pigments increased in value for 2 to 3 weeks, then remained constant, due apparently to decreasing production; the initial increase was much more rapid when the gall bladder was removed at the time of the production of obstruction to the common bile duct. It was also found that ascites would appear when the animals were put on a protein diet and that it disappeared on resumption of a carbohydrate diet. It is not yet known definitely whether bile pigments or bile acids are the toxic factor in jaundice. It was the finding of King and Stewart that the injection of the pigment and not the salts of bile produced bradycardia and low blood pressure. The finding of bilirubin in the tissues does not necessarily mean, of course, that it is alone responsible for the parenchymatous damage observed. Haessler, Rous, and Brown found that the elimination of bile pigment during jaundice was markedly increased in the dog by "flood diuresis" with intravenous saline solution; the effect on the bile salts was unknown. No such effect was obtained by diuresis from water by mouth, but these authors felt that accumulation of bile pigments might be diminished by such diuresis. The "flood diuresis" was produced with saline solution introduced at such a rate as to be prohibitory in clinical use. They give a very thoughtful discussion of the significance of jaundiced epithelial cells in the urine sediment as evidence of renal injury. Wangensteen and his co-workers investigated the effect of repeated administration of ether and chloroform on output of phenolsulphonephthalein following experimental obstruction of the common bile duct in dogs. They found no evidence of impairment of kidney function, nor did anuria develop; the urea nitrogen showed a terminal rise in only 2 of 16 dogs.

This raises the question of the interpretation of renal function tests in cases in which both kidney and liver damage is suspected. Hanner and Whipple produced characteristic lesions of the liver by chloroform and phosphorus and in other cases produced obstructive jaundice in dogs. They then found in all cases an increase in phthalein excretion by the kidneys. They explained this by assuming that the 10 or 15 per cent of phthalein excreted through the bile by the healthy liver was shunted through the kidneys when liver function was grossly impaired. Their conclusion was that an abnormally high phthalein output in the presence of healthy kidneys should make one suspicious of serious impairment of liver function. For our own purposes, this adds to the value of the test. However the kidneys may be badly damaged in biliary infections with or without jaundice and without serious impairment of liver reserve, in our opinion, though our own clinical cases are not reported in such a way as to offer conclusive evidence in support of that opinion. Case 13 (aged 53 years) on the other hand, with gross and microscopic evidence of hepatitis and phthalein excretion of 85 per cent in 1 hour after intravenous injection, probably is a case which fairly bears out the contention of Hanner and Whipple. In their paper they quoted Moller and Lunsgaard as reporting a delay and decrease in phenolsulphonephthalein excretion in patients with hepatic disease; these cases are spoken of by Chabanier and Gaume in the paper as having had evidence of renal insufficiency. The subject must be regarded as being still controversial, especially in view of the fact that Hanner and Whipple's work is based on animal experimentation.

Wakefield, Power, and Keith have recently reported a large series of determinations of inorganic sulphates of the blood by an original volumetric method as a criterion of early renal insufficiency in chronic nephritis. Their cases are carefully and fully presented and merit close inspection. They found the sulphates increasing before a fall in phenolsulphonephthalein excretion. The closest correlation existed between the behavior of the sulphates, the "urea clearance" test of Van Slyke, and the specific gravity of the urine as determined by the concentration-diuresis test of Volhard and Fahr. It will be interesting to see whether this method of sulphate determination will give us warning of impending kidney insufficiency in gravely sick patients with diseases of the biliary tract.

We have depended on examination of the urine, determination of blood non-protein nitrogen, phthalein excretion, and various modifications of the Volhard and Fahr concentration-diuresis test in our estimations of the anatomical and func-

tional state of the kidneys; it has not been possible to do them all or to repeat them at will in many of our patients. We have felt that more dependable results are obtained by injecting phthalein intravenously rather than intramuscularly, since absorption rate must vary considerably from subcutaneous tissue, fat, and muscle into which the dye is variously deposited by different individuals. In clinical practice, it is essential that voided specimens from women be uncontaminated; every detail of the test, indeed, must be closely checked if one hopes to have valid records of progress. In the presence of jaundice, color matching with the standard is frequently impossible unless bile pigment be removed from the urine by one of the various methods. We find the ability to concentrate urine more satisfactory as a functional test and closely controlled research and experimental work by many workers has shown it to be of great value (10). We have not been interested in the ability of these patients to show diuresis, since the cases that develop suppression of urine excrete urine of low specific gravity; we have tested only their ability to concentrate, therefore. Here again, carrying out of a formal concentration test involving the withdrawal of fluids for a period of 15 hours or so is usually out of the question from a therapeutic point of view with patients who are acutely ill. In such cases, the phthalein excretion is more widely useful. Until recently, we have performed concentration tests with the patient on bed rest and on general hospital diet, with or without meat, previous to the test. At 6:00 p.m. to 6:00 a.m. as one specimen; from 6:00 a.m. to 9:00 a.m. all urine is collected as a second specimen; the amount and specific gravity (by hydrometer) of both specimens is then measured. Patients whose kidneys we regard as being entirely normal do not ordinarily have a specific gravity below 1,015 or above 1,020 for the second specimen. This has seemed to us an inadequate method, since the specific gravity of the combined specimens from 6:00 a.m. to 9:00 a.m. tells us nothing of the specific gravity of any of them unless the total quantity be quite small (less than 100 cubic centimeters) which is not usually the case. We have more recently, therefore, had the patient attempt to void at 7:00 a.m., 8:00 a.m., and 9:00 a.m., and catheterized for the final specimen if unable to void; these specimens are saved as separate ones. In this way we obtain one or two specimens of only an ounce or two for our final specimens and if such are not concentrated we can feel assured that some functional renal impairment exists.

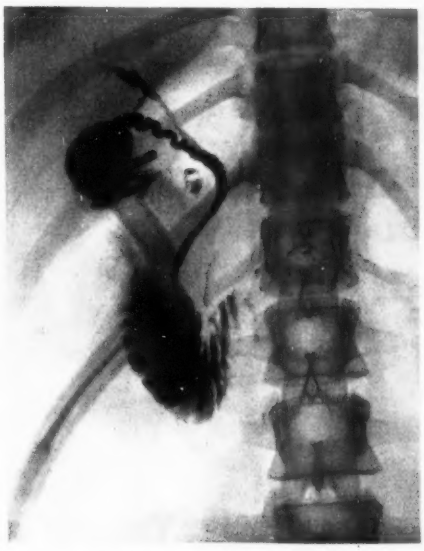

Fig. 1. Case 7. January 2, 1931, injection through Pezzar catheter in gall bladder. Preliminary cholecystostomy, November 20, 1930. Note normal cystic duct, small patent common duct. Subsequent cholecystectomy without exploration common duct, was done March 24, 1931.

Quantities of urine less than one ounce are accurately diluted with water to an amount the specific gravity of which can be measured by the hydrometer. We have not had sufficient experience with this method to have set up an arbitrary standard of normal, but it is our impression that one of the specimens after 6:00 a.m. should go above a specific gravity of 1,020 on this regimen with normal kidneys. We are aware of the many factors, such as humidity, temperature, and emotional states, which influence the output of water through the kidneys and we attempt to take them into account as fully as possible in interpreting the results of these tests.

We are presenting the following 13 case records of patients with disease of the biliary tract that were, or had once been, amenable to surgery. Cases 1 to 6 are those who developed suppression of urine with other signs of nephritis; Case 12 probably belongs in this group also, though his urinary output was not recorded. Cases 1, 6, 7, 8, 9, and 10 are submitted as those in whom a graded operation was planned, cholecystostomy with maintenance of drainage for several months by Pezzar catheter being the preliminary steps. Cases 11, 12, and 13 are

Fig. 2. Case 8. May 9, 1931, injection through Pezzar catheter in gall bladder. Preliminary cholecystostomy September 18, 1930. Note complete obstruction common duct, dilatation cystic, common, and intrahepatic tree. Subsequent cholecystectomy and exploration common duct, May 14, 1931.

patients in whom no further operation than cholecystostomy was contemplated.

Case 1. Mrs. M. S., age 57 years, admitted to the hospital, November 25, 1928, complaining chiefly of abdominal pain, jaundice, vomiting. First gastro-intestinal symptoms appeared 5 years previously with attacks of severe pain in right upper quadrant, vomiting, deep jaundice, clay colored stools. Patient could not get back to normal duties for 6 months. Health has been fair since, with intermittent attacks, mild pain, acholic stools, and constant belching and fullness after meals. She has not suffered a loss of weight. Present attack was of 2 weeks' duration; no urine was voided for 24 hours before entrance.

Examination revealed an obese, elderly woman in considerable pain; nauseated, fairly alert; skin and sclera slightly yellow; obvious dehydration; heart slightly enlarged to left, regular, sounds distant; blood pressure, 160/72; pendulous abdomen; right rectus spastic; marked tenderness and inhibition right upper quadrant; a tender mass size of grapefruit and dull to percussion is palpable; liver not felt; temperature, 98 degrees; pulse, 108; respiration, 18; white blood cells, 36,000; vomitus contained bile.

Patient was given hypodermoclysis of 1,600 cubic centimeters of saline on night of admission, morphine, and gastric lavage. She did not thereafter have enough pain to require morphine. At 7:00 a.m., November 26, she voided ½ ounce for the first time in 36 hours. Hypodermoclysis was resumed and 50 per cent glucose was given intravenously. She was catheterized 4 hours later and there was obtained ½ ounce of dark yellow urine, acid, showing 2 plus albumin, no bile, numerous white blood cells and red blood cells, occasional coarsely granular casts, and numerous bacteria. During the rest of the day she voided 84 cubic centimeters. Total output was 124 cubic centimeters for the 30 hours since admission with an intake of 3,700 cubic centimeters by hypodermoclysis of 1,600 cubic centimeters of blood, and 500 cubic centimeters of 50 per cent glucose intravenously. At this time white blood corpuscle count was 32,000 with 86 per cent polymorphonuclear, red blood corpuscles, 5,000,000, hæmoglobin, 98 per cent; non-protein nitrogen, 52; icterus index, 15; blood pressure, 142/80. During that night she voided total of 270 cubic centimeters with an intake of 2,100 cubic centimeters under the skin. The following day she again received 50 per cent glucose intravenously and 1,500 cubic centimeters hypodermoclysis and the urinary output suddenly rose to 1,730 cubic centimeters in 24 hours. Urinalysis on November 26, showed 1 plus albumin; acid; specific gravity, 1,005; numerous white blood corpuscles and red blood corpuscles; a moderate number of coarsely granular casts; acetone, negative. White blood corpuscle count had dropped to 9,000; temperature became normal, with pulse averaging 86. November 28, fluids in small amounts were started by mouth and the urinary output continued to exceed the fluid intake until December 4, there being considerable diuresis at night and there having been no demonstrable œdema at any time. November 28, the non-protein nitrogen was 63; blood pressure, 140/70. December 1, non-protein nitrogen was 45; blood pressure, 210/96; and electrocardiogram showed normal curves. December 8, non-protein nitrogen was 44; blood pressure, 160/80. December 1, catheter urine specimen showed reaction acid; specific gravity, 1,005; trace albumin; a few white blood corpuscles, and bacteria. December 3, white blood corpuscles numbered 9,800. December 6, icterus index was 16. There was no nausea after December 5 but a persistent sensation of abdominal fullness and belching was noted.

Operation was done December 11. Nitrous oxide gas plus novocain infiltration and block anæsthesia was used. An enormous gall bladder filled with thick black bile and stones was aspirated, sutured to peritoneum, and a large soft rubber tube sutured into the gall bladder for drainage; no exploration was attempted.

The postoperative course was uneventful except for considerable lagging of urinary output behind the fluid intake during the first 2 days. Patient was discharged December 29, 1928, with a small amount of seropurulent drainage around the tube. Bile drainage was prompt following operation and decreased in amount after the first few days, not exceeding 200 cubic centimeters each 24 hours during the final week in the hospital. During the first 2 weeks after discharge patient passed twelve stones through the tube which came out 6 weeks after operation and was not replaced. Stools were of normal color at all times. There was a small but constant amount of drainage from the fistula; the belching and sensation of fullness disappeared; and there were no pain, chills, or jaundice.

Patient was readmitted to the hospital June 25, 1929, having been for 1 week on a 1,000 calorie diet with thyroxin, grain 1/80, daily. Reduction regimen continued for 1 week after entrance. Catheter urine showed reaction acid; specific gravity, 1,017; slight trace of albumin; occasional white blood corpuscles; hæmoglobin normal; temperature, pulse, and respiration, normal; blood pressure, 160/80.

Operation was done June 25, 1929. Nitrous oxide and novocain infiltration and block anæsthesia were used. The abdomen was opened just lateral to the old scar; the gall bladder was moderately thickened; it was aspirated

Fig. 3. Case 10. February 2, 1931, injection through Pezzar catheter in gall bladder. Preliminary cholecystostomy July 29, 1930. Common duct apparently normal, emptying promptly. Subsequent cholecystectomy not yet done (see text).

Fig. 4. Case 14. October 31, 1930, injection through T-tube in common duct. Excision stricture and choledochostomy December 10, 1929. Note persistent dilatation of common duct and intrahepatic radicals. T-tube removed December 4, 1930.

and packed; the ducts appeared normal in size and thickness. Cholecystectomy was performed with drainage to stump of cystic duct.

The postoperative course was entirely uneventful. The urine output was good at all times. Patient was discharged July 11, 1929. On April 3, 1932, she was reexamined. Digestion has remained excellent; no pain or jaundice; regained weight to 203 pounds during past winter, but has recently developed toxic adenoma thyroid and diabetes mellitus and weight has fallen to 165 in the past 4 months.

Case 2. Mrs. M. B., aged 58 years, was admitted April 5, 1929. The chief complaint was jaundice with continuous vomiting. Onset of jaundice 1 month ago with mild pain in both upper abdominal quadrants, nausea, and vomiting with increasing severity, incontinence of urine and fæces, stuporous past 48 hours. Past history was not obtained.

Examination revealed an obese elderly woman, deeply jaundiced, stuporous, obviously dehydrated; marked fetor oris; teeth poor; lungs entirely clear; heart rapid, regular, size uncertain, sounds rather distant, no murmurs; blood pressure, 105/52. The abdomen had no scars; both upper quadrants and epigastrium were tender and spastic; the liver was not palpable; no masses were felt; the pelvis was not examined; no œdema of extremities; temperature, 99.2 degrees; pulse, 115; respiration, 24. The catheter urine was dark brown; acid; specific gravity, 1,009; 3 plus albumin; bile, positive; moderate number red blood cells, a few white blood cells and granular casts.

Immediate blood transfusion was given and intake maintained by hypodermoclysis of saline and 10 per cent glucose intravenously. Small nasal tube was introduced into the stomach and left there, 150 cubic centimeters of orange juice being inserted every 3 hours. Intake from entrance for 20 hours: nasal tube, 750 cubic centimeters; hypodermoclysis, 2,800 cubic centimeters; intravenous, 1,000 cubic centimeters; total, 4,550 cubic centimeters. Output: she vomited small amounts twice, urine was voided involuntarily twice in very small amounts; per catheter, 180 cubic centimeters; total ? April 6, white blood corpuscles were 13,000; red blood corpuscles, 5,250,000; hæmoglobin, 100; non-protein nitrogen, 53; icterus index, 130; urine, many red blood cells and 1 plus albumin; pulse, 85; blood pressure, 118/65. Patient was still stuporous. Twenty-four hour intake: mouth, 2,300 cubic centimeters; hypodermoclysis, 3,600 cubic centimeters; intravenous, 100 cubic centimeters (50 per cent glucose); total 6,000 cubic centimeters. Output: stomach syphonage, 1,350 cubic centimeters; urine, 610 cubic centimeters per catheter; total 1,960 cubic centimeters. April 7, patient failed rapidly, temperature stayed normal, and pulse was under 100 until 2 hours before death at 6:50 p.m. Marked œdema developed around eyes and moist bronchial râles appeared at 11:00 a.m., blood pressure 168/90 at this time. No precordial friction rub was heard. Intake from 7:00 a.m. until 6:50 p.m.: mouth, 540 cubic centimeters; hypodermoclysis, 1,000 cubic centimeters; 50 per cent glucose intravenously, 50 cubic centimeters; total, 2,190 cubic centimeters. Output: syphonage, 1,425 cubic centimeters; urine, 250 cubic centimeters per catheter; total 1,675 cubic centimeters. Autopsy was performed immediately following death. Moderately increasing bile stained fluid was found in pericardium and peritoneum; there were hæmorrhages into the wall of the small intestine and cæcum amounting almost to gangrene; the

Fig. 5. Case 15. June 10, 1932, injection through T-tube in common duct. Cholecystectomy and choledochostomy May 28, 1932. Note dilatation common duct and intrahepatic radicals, with prompt emptying though patient in Trendelenburg position.

appendix was densely fixed in old adhesions and contained one fæcalith; the liver was rather small with dilated ducts; gall bladder hydropic and adherent to stomach; foramen of Winslow obliterated; no stone in common duct; a hard mass size of lemon in head of pancreas; right kidney weighed 175 grams, left a little less, surfaces smooth, capsules stripped easily; cut surfaces showed well defined cortex and medulla, petechial hæmorrhages into renal pelves; heart negative except for deep jaundice which all organs showed. All parenchymatous organs, stomach, duodenum, and pancreas were saved for microscopic examination but were misplaced and no report of them is available.

Case 3. Mrs. H. F., age 71 years, admitted December 14, 1931. Her chief complaint was jaundice and indigestion. Eight years ago she had had attacks of nausea, vomiting without pain or jaundice over a period of 2 months. Five years ago she had an attack of severe pain in the upper abdomen and chest radiating to back, lasting 3 days and associated with much nausea, nocturia once or twice nightly for past year increasing to 4 or 5 times in past 6 months. Six months ago she had noted onset of weakness, but loss of less than 10 pounds; clay colored stools for 2 months; œdema of legs to groins for 2 weeks; nausea and belching, but no vomiting or pain; some palpitation past 2 weeks; no orthopnœa or dyspnœa. She was confined to bed for past 2 weeks without improvement. Very small doses of digitalis were given for 1 week before admission. The onset of jaundice has been so gradual that it cannot be definitely dated.

Examination revealed a stout elderly woman, alert, not in pain. The skin was a peculiar bronze, the sclera yellow; the heart was not enlarged, the apex impulse was somewhat diffuse, the sounds were clear, regular, of good quality with no murmurs, an occasional extrasystole. Blood pressure was 140/75; the lungs were negative. The abdomen showed no scars; the wall was relaxed; the right lobe of the liver was felt 3 finger breadths below right costal margin, edge rounded, perhaps irregular, and slightly tender. The gall bladder was palpable, tender. No free fluid demonstrable. The back showed slightly pitting œdema over lumbar and sacral regions. The pelvis and rectum were not examined. Pitting œdema noted of both legs to knees. No varices were noted in legs or abdominal wall. Temperature was 96.2 degrees; pulse, 82; respiration, 22. Catheter specimen of urine was acid; specific gravity 1,009; bile, positive; very occasional red blood corpuscle and cocci; hæmoglobin 77 per cent; red blood cells 4,200,000; white blood corpuscles, 7,600; differential (Schilling)—eosin, 3; stabs, 28; segmented, 42; lymphocytes, 22; large mononuclears, 5; icterus index, 6; van den Bergh, positive, direct reaction; stool, negative for bile and for occult blood. Intravenous iso-iodeko- gave no gall-bladder shadow but there were characteristic shadows of stones in gall-bladder area. Forty-two per cent of the dye was retained in the blood 30 minutes after injection. Electrocardiogram showed T-waves broad and flat in all leads and left axis deviation.

Impression: Obstructive jaundice due to (silent) stone in common duct or, less likely, pressure on common duct from carcinoma of gall bladder. The œdema was thought to be due to myocardial failure with incomplete digitalis effect.

Patient was put on limited fluid intake with salt-free diet high in carbohydrate; on December 10 the œdema of the legs and back had almost completely disappeared and the liver was barely palpable. During this 24 hour period, however, she voided only 40 cubic centimeters. Tincture of digitalis, 1 cubic centimeter every 4 hours, was started as a diuretic although the pulse was 80. December 17, patient was weak, drowsy, complaining of visual disturbance. Fifty per cent glucose was given intravenously with insulin and blood transfusion. Total intake was 1,500 cubic centimeters. Output urine was 170 cubic centimeters, and there was again considerable œdema of the back. December 18, non-protein nitrogen was 47; icterus index, 75; catheter urine, acid, specific gravity 1,012, 2 plus albumin, bile positive, numerous white blood corpuscles, and bacteria. Intake 2,100 cubic centimeters. Output 410 cubic centimeters after 1 cubic centimeter of salyrgan intravenously. December 19, 2 cubic centimeters salyrgan was given intravenously in 50 per cent glucose with insulin and repeated daily thereafter. Catheter urine showed reaction, acid; specific gravity 1,005; 3 plus albumin; bile positive; a few red blood corpuscles, and a moderate number of white blood corpuscles. Intake was 1,600 cubic centimeters. Output was 480 cubic centimeters. December 20, patient was quite drowsy, considerably weaker, œdema legs and back was increasing, but no ascites or pulmonary œdema were noted. Digitalis was discontinued since the pulse remained about 70. An indwelling catheter was inserted in order to keep track of the urinary output as patient was beginning to void involuntarily. Stools were light brown for the first time and were faintly positive for bile, which was present thereafter until death. Icterus index was 110. Carbon dioxide combining power was 38.5 volume per cent; blood chlorides, 510 milligrams. December 21, intake was 2,170 cubic centimeters, output 780 cubic centimeters. The urine was unchanged. Temperature, pulse, and respiration remained normal; blood pressure 110–60. December 22, patient was quite stuporous. Intake was 1,380 cubic centimeters, output was 560 cubic centimeters. The urine was acid.

specific gravity 1,005; 3 plus albumin; numerous red blood corpuscles, white blood corpuscles, and bacteria. December 23, patient expired.

Permission for autopsy limited to abdomen was obtained. The findings are to be reported in detail in another paper: primary adenocarcinoma of the liver cells (malignant hepatoma) with small organoid metastases to the lungs, periportal fibrosis, chronic cholecystitis with cholelithiasis, marked dilatation of common duct with small fresh ulceration of mucosa (stone not found in duct or in intestine), small retention cysts in pancreas, slight necrosis of peripancreatic fat, chronic perisplenitis, cloudy swelling of the kidneys with deposit of albuminous material in the glomerular capsules and in the tubules, marked jaundice of viscera. The heart was examined through an incision in the diaphragm; it was not grossly enlarged and the muscle was soft. There was a moderate amount of bile-stained fluid in both pleural cavities and a small amount in the peritoneal cavity.

CASE 4. Mr. L. P., aged 53 years, was admitted to the hospital April 2, 1932. Patient had been under observation as an ambulatory case until the night before entrance. The referring physician had studied him exhaustively a month previously with complete gastro-intestinal and gall-bladder X-rays, blood chemistry, electrocardiograms, etc., and a final diagnosis of cholecystitis with cholelithiasis had been made. The urine had then been normal and phenolsulphonephthalein excretion was 75 per cent in 2 hours after intravenous injection. There was a history of epigastric pain, abdominal fullness, and belching after meals, in spells, for about 10 years. Constant jaundice, varying in degree, had been present for 2 months before admission; clay colored stools for 1 month; swelling of abdomen (ascites) for 10 days; œdema of ankles for 4 days. On admission there was noted a deep jaundice of the skin and sclera. Patient was somewhat drowsy; lips and nails were cyanotic; audible moist râles were noted throughout bronchial tree. Percussion note was dull in lower axillæ and posteriorly. The apex impulse was diffuse in fourth intercostal space, 5 centimeters to left of sternum; sounds faint and regular, no murmurs. The abdomen was distended; shifting dullness present in both flanks. There was slight tenderness in the right upper quadrant and epigastrium; no masses or viscera were palpable. Pitting œdema noted in lower anterior abdominal wall and back. The genitalia and rectum were negative. Pitting œdema noted in feet and ankles. Temperature was 100 degrees, pulse, 128; respiration, 24; blood pressure, 115/60. Catheter urine showed acid reaction, 3 plus albumin; bile positive; a few hyaline and granular casts, moderate number red blood cells, a few white blood cells and bacteria; hæmoglobin 62 per cent; red blood count 3,000,000; white blood count 8,000; differential (Schilling) basophiles, 1; Young, 45; stab, 30; segment, 12; lymphocytes, 10; icterus index, 60.

In the first 36 hours, April 2 to 4, only 160 cubic centimeters of urine was passed with fluid intake of 2,000 cubic centimeters of 5 per cent glucose intravenously, and a negligible amount by mouth and proctoclysis. When we first saw the patient on the morning of April 4 he was quite stuporous, physical findings had not changed since admission, blood pressure 118/60; pulse, 124; respiration, 24; and it was our impression that he had in addition to obstructive jaundice a nephritis which was responsible for his œdema rather than circulatory failure. Non-protein nitrogen was 68; uric acid 4.4. An attempt was made to start diuresis with salyrgan and 50 per cent glucose intravenously which were repeated 12 hours later; 450 cubic centimeters of blood was given as transfusion and oxygen started continuously by nasal catheter. Only 210 cubic centimeters were obtained before death which occurred on the morning of April 5. Until shortly before death pulse remained around 120, respiration 24, temperature slightly subnormal. Permission for autopsy was refused.

CASE 5. Miss M. B., aged 61 years, admitted to hospital April 4, 1928. Her chief complaint was increasing jaundice and abdominal pain. The first attack of severe pain in the right upper quadrant of the abdomen occurred 14 years ago with bloating and fullness after meals. She had had several similar attacks of colic during the next 4 years; none for the past 10 years though indigestion continued. Two weeks ago she had a sharp attack of pain followed the next day by jaundice which has steadily increased with clay colored stools and considerable vomiting. No vomiting had been noted for past few days.

Examination revealed an obese elderly woman, deeply jaundiced, not in pain, quite nervous, belching frequently. The heart was slightly enlarged to left. The abdomen was quite tender under the right costal margin; otherwise negative. The temperature varied from normal to 99.9 degrees, pulse varied from 68 to 110 with the temperature. April 5, hæmoglobin was 85 per cent, white blood cells 6,000; clotting time 5 minutes; icterus index, 150; van den Bergh, immediate direct reaction; urine, acid, specific gravity 1,015, faint trace albumin, bile positive, numerous leucocytes, a few hyaline and granular casts.

She was given intravenous glucose on admission. April 6, blood transfusion; calcium chloride was given intravenously on three successive days. She was put on a high carbohydrate diet. There was inconstant nausea; no vomiting; stools of normal color after April 6. Temperature came back to normal on April 8 and went up to 100 on April 10 and to 101 degrees on April 16. It was thereafter normal. April 13 iodekon by mouth gave an uncertain hazy shadow in gall-bladder region. Icterus index 150 on admission, 180 on April 7, 100 on April 10, and 60 on April 14. Non-protein nitrogen was 42 on April 7, April 16, white blood cells were 6,000, clotting time $4\frac{3}{4}$ minutes.

Operation was done April 21. Ether and novocain infiltration and block anæsthesia were used. The gall bladder was cystic, the common ducts thickened, enlarged, and buried in dense adhesions. One mulberry pigment stone was found in the gall bladder. The common duct was opened, and careful exploration revealed no stone or obstruction. There was free passage into duodenum. A catheter was sutured into the hepatic duct. A drainage tube was sutured into the gall bladder in view of patient's age and rather poor condition. Penrose drain was inserted into the common duct. Pulse was 94 at conclusion of operation.

Postoperative course. Temperature was 103 degrees night of operation and 101 degrees the following morning. April 23, pulse suddenly went from 100 to 160. Heart action was regular. Blood pressure was 110/80, the preoperative level, and there was a suggestion of pulsus alternans. Respiration was 24. Patient was digitalized on advice of consultant, with massive doses, and was then maintained on digitalis thereafter. Pulse returned to 90 that night and was usually between 80 and 90 thereafter. Bile drainage was immediate, averaging 600 cubic centimeters in 24 hours for 1 week. Stools were of normal color until eighth day after operation, April 29; they were continuously clay colored thereafter until death. A moderate amount of bile-stained drainage continued on the dressings but no digestion of skin occurred. Following operation water intake was maintained by mouth, 2,000 to 2,500 cubic centimeters daily. The urine on day after operation showed faint trace of albumin, specific gravity, 1,024, and was normal microscopically. Urinary output declined steadily from 800 cubic centimeters in 24 hours to less than 500 cubic centimeters daily. This was not noticed

until April 26 when patient began to complain of urgency which responded to symptomatic treatment. April 26 specific gravity was 1,014, faint trace albumin, bile positive, numerous white blood cells, a few hyaline and granular casts. Fluid intake thereafter was pushed beyond 3,000 cubic centimeters daily and blood transfusion was given. The urine output fell to between 350 and 450 cubic centimeters daily, however, until death. April 28 temperature rose to 102 degrees, then gradually fell to subnormal where it remained until the day of death. April 30 non-protein nitrogen was 60, urine showed heavy trace of albumin, bile positive, a few red blood cells and white blood cells, and small bacilli. No further laboratory examinations are reported until death which occurred on May 6, 1928. Patient was restless and disoriented during the last week. Permission for autopsy refused.

CASE 6. Mrs. C. K., aged 63 years, was admitted to the hospital October 29, 1930. She had had an attack of nausea and vomiting one year ago with burning sensation in epigastrium lasting 2 days. She had suffered from fullness and belching after eating since then. Forty-eight hours ago burning pain in epigastrium and right upper quadrant recurred and vomiting of bile-stained fluid started. Pain was continuous, shifting 12 hours ago to right lower quadrant; vomiting was intermittent. Stools were normal and daily during present illness. There were no cardiorespiratory or genito-urinary symptoms; no chills or jaundice. She was given morphine by referring physician before she was sent 75 miles to hospital with diagnosis of acute appendicitis.

Examination revealed an obese, elderly woman mentally alert, but very tired, in moderate pain; skin and sclera normal; head and neck negative except for dry tongue; heart enlarged somewhat to left, sounds of good quality. A snapping, occasional extrasystole was noted. The lungs were slightly emphysematous. The right rectus muscle was in moderate spasm. There was marked respiratory inhibition. The liver edge was palpable 3 to 4 finger breadths below the rib margin on the right. Continuous with it there was a tender, tense mass the size of a lemon extending to the level, and to the right of the umbilicus, and moving with respiration. Pelvic examination revealed no tenderness or induration on either side. Temperature was 98.4 degrees; pulse, 86; and respiration, 20; blood pressure, 140/85; white blood cells, 34,000. Catheter urine, showed acid reaction, 2 plus albumin, many hyaline and finely granular casts, occasional white blood cells, no organisms; non-protein nitrogen 37. A flat film of the abdomen showed clearly a gall-bladder shadow at site of the tender mass. Impression: empyema of gall bladder. Patient was put on peritonitis treatment with nothing by mouth: 3,000 cubic centimeters saline solution as hypodermoclysis, 1,000 cubic centimeters 10 per cent glucose intravenously in the 16 hours until the morning following admission. During this time she voided 150 cubic centimeters of urine. October 30, white blood cells were 25,500; temperature, 99.8 degrees; pulse, 96; respiration, 24. Patient felt greatly rested.

Operation was done October 30. Nembutal, grains 3, was given intravenously, nitrous oxide and local infiltration and block anæsthesia being used. Through a short, high right rectus incision the abdomen was opened. The peritoneal fluid was found to be bile-stained and greatly increased in amount. The gall bladder was freed from the omentum. It was the size of a small coconut, greatly thickened, and dark blue in color. It was lifted into incision and attached to fascia with Allis clamps and aspirated of thick blue green bile and many tiny stones. A Pezzar catheter was introduced, one plain gauze pack and two small iodoform packs were left in the wound around the gall bladder to create adhesions. Closure to packs and tube, the clamps being left in place. A note was made on the operative chart that patient was to wear the Pezzar catheter for 6 months and then have a cholecystectomy. At end of operation pulse was 120, respiration 28; blood pressure, 132/70. Blood transfusion was given immediately and peritonitis treatment resumed for 24 hours. During this period with a total intake of 3,200 cubic centimeters the output of urine was 785 cubic centimeters. Temperature was 101.2 degrees; pulse, 100; and respiration, 28, the night of operation gradually returned to normal in the next 3 days. She was put on soft diet on the third day. There was immediate bile drainage, not exceeding 100 cubic centimeters per 24 hours. Stools were normal in color at all times. Gauze packs were removed at intervals until the twelfth day. Patient was to be allowed up on November 13, but that morning she developed a left-sided bronchial pneumonia of which she died November 21. Permission for autopsy refused.

CASE 7. Miss L. M., aged 37 years, was admitted to hospital November 13, 1930. Since appendectomy for ruptured appendix 6 years ago she has had spells of minor upper abdominal discomfort especially after eating raw fruit. Four weeks ago there was a sudden onset severe pain in the right upper quadrant and epigastrium, the pain radiating around the rib margin to the right scapula; there were considerable vomiting, fever, and onset of jaundice. Morphine was required to relieve pain. She vomited 2 to 3 times daily for 2 weeks, once daily since then. Jaundice gradually subsided; she had had no chills; uncertain as to acholic stools. The past history was negative except for scarlet fever and diphtheria when a child. Examination revealed a short, rather obese woman, not in pain, skin slightly yellow, sclera clear; head, neck, heart, and lungs negative; blood pressure 135/85. There was an old low right rectus scar, healed by secondary intention; no distention or spasm, moderate tenderness in epigastrium and right upper quadrant; slight inhibition; no masses or viscera palpable. Pelvis and rectum not examined. Temperature was 98 degrees; pulse, 88; and respiration, 18. Catheter urine showed acid reaction, specific gravity 1,014, faint trace of albumin, bile negative, sediment negative; hæmoglobin 83 per cent; white blood cells 6,000; differential (Schilling) normal; icterus index 5.1. Impression: chronic cholecystitis with subsiding acute exacerbation, question of stone in common duct. November 14, phenolsulphonephthalein 540 cubic centimeters, 45 per cent in 2 hours (intramuscular). Because of history of definite changes in color of stool during first week of attack it was felt that her common duct would have to be explored. Because of her thick, peculiarly deep thorax and abdomen this promised to be very difficult; it was felt that her phenolsulphonephthalein excretion should improve before undertaking so radical a procedure.

November 18, urine concentration test 6 p.m. to 6 a.m.: ? cubic centimeters, specific gravity 1,010; 6 a.m. to 9 a.m.:? cubic centimeters, specific gravity 1,008. Phenolsulphonephthalein 230 cubic centimeters, 37.5 per cent in 2 hours (intramuscular). November 19, phenolsulphonephthalein 680 cubic centimeters, 37.5 per cent in 2 hours (intramuscular). With this definite evidence that kidney function was far from normal we informed patient that she could either wait until kidney function improved with the risk of further attacks of colic in the meanwhile or have cholecystostomy performed at once with subsequent cholecystectomy and exploration of common duct. She preferred the latter course.

Operation was done November 20. Phanadorn, grains 15, was given preliminary to operation. Nitrous oxide plus local infiltration and block anæsthesia were used.

Through a lateral right rectus incision the fundus of the gall bladder was brought into the wound and anchored with Allis clamps and a Pezzar catheter was inserted into it. Clamps were left in place for 48 hours.

Postoperative course was uneventful for 9 days. The urinary output good. Immediate bile drainage was from 100 to 300 cubic centimeters per 24 hours; when it exceeded 200 cubic centimeters, it was injected into rectum was retention enema; patient in chair on seventh day. On ninth day developed thrombophlebitis on left saphenous vein. This improved on the usual treatment. December 11, 1930, she was discharged. The incision was healed to the catheter. January 1, 1931, she was readmitted to have Pezzar changed. She has had two attacks of colic similar to those before operation but they were much less severe and without jaundice; the stools have remained normal in color. Temperature, pulse, and respiration were normal; blood pressure 120/80. Urine concentration test showed 6 p.m. to 6 a..m: ? cubic centimeters, specific gravity 1,002; 6 a.m. to 9 a.m., ? cubic centimeters; specific gravity 1,014. Phenolsulphonephthalein output was 155 cubic centimeters, 47.5 per cent in 2 hours (intramuscular). Voided urine showed reaction alkaline, 1 plus albumin, moderate number white blood cells, a few red blood cells. Lipiodol injection into catheter showed no obstruction in the common duct and prompt emptying into duodenum. February 16 she was readmitted to have the Pezzar changed. She had had entire comfort until a week ago when the catheter began to slip out of the gall bladder and with partial blocking of fistula the gall bladder became tender, red, and there was a slight purulent discharge. Temperature, pulse, and respiration were normal; blood pressure was 120/80. The urine concentration test showed 6 p.m. to 6 a.m.: ? cubic centimeters, specific gravity 1,017; 6 a.m. to 9 a.m.: ? cubic centimeters; specific gravity 1,013. Phenolsulphonephthalein: 185 cubic centimeters, 42.5 per cent in 2 hours (intramuscular). Lipiodol injection into catheter showed common duct patent and emptying promptly. March 18, 1931, she was readmitted for cholecystectomy, having felt well in all respects except for occasional soreness about the tube. Lipiodol injection gave results as before with no dilatation of hepatic or common ducts. March 19, concentration test showed: 6 p.m. to 6 a.m., 525 cubic centimeters; specific gravity 1,010; 6 a.m. to 9 a.m., 60 cubic centimeters; specific gravity 1,011. Phenolsulphonephthalein: 720 cubic centimeters, 53 per cent in 2 hours (intramuscular). March 23, concentration test 6 p.m. to 6 a.m., ? cubic centimeters; specific gravity 1,000; 6 a.m. to 9 a.m., ? cubic centimeters; specific gravity, 1,008.

Operation was done March 24. Nitrous oxide gas and anæsthesia was used with ethylene novocain block of abdominal wall. Through a right rectus incision between the midline and fistula the common and hepatic ducts were found to be normal in size and consistency; no stones were felt and the ducts were not opened; gall-bladder wall was 1 inch thick on the peritoneal aspect; it was removed and a small gauze pack partially surrounded by rubber was placed against the liver bed and brought out old fistula.

After operation the urine output was satisfactory at all times, approximating the intake after the first 24 hours. The course was uneventful except for considerable purulent drainage from the sinus for several days after removal of packs and drains. No bile drainage was used. April 13 patient was allowed up. She elected to stay in the hospital until the sinus had completely granulated. April 26, 1931, she was discharged. March 30, 1932, she felt excellent; was eating everything with good digestion until past December when she weighed 153; has since developed symptoms of thyrotoxicosis and has lost 10 pounds. Pulse was 116, blood pressure 155/95. Patient refused to remain for complete examination, but it is our impression that she has not only a toxic goiter but definite renal damage in view of high diastolic pressure.

Case 8. Mrs. D. M., aged 63 years, was admitted to hospital August 31, 1930. She had been entirely well until 1 month ago, at which time there was an onset of severe pain in the right upper quadrant, radiating to back, and she became jaundiced; had a sensation of fullness, she belched after meals, and had pain which continued intermittently. She vomited several times with attack 3 days ago. The stools were frequently clay colored. Her past history was uneventful except for malaria 4 years ago. Her average weight was 170 pounds.

Examination revealed a moderately obese, elderly woman in slight pain with slight jaundice of skin and sclera; heart and lungs negative; abdomen flabby, fat; positive inhibition; moderate tenderness in right upper quadrant and epigastrium; no masses or viscera were palpable; extremities were negative; weight 150 pounds. Temperature was 99.4 degrees; pulse, 88; and respiration, 22. September 2 red blood cells were 4,870,000; white blood cells, 9,400; hæmoglobin 70 per cent; differential, normal; icterus index, 12.1; non-protein nitrogen, 30.9. September 3, temperature returned to normal and a glucose tolerance curve was normal; no spilling of sugar. Urine concentration test was performed but the specimens were mislaid and no report was available. September 5, icterus index, 10; catheter urine acid, faint trace albumin, bile positive, a few red blood cells and white blood cells; phenolsulphonephthalein 400 cubic centimeters, 75 per cent in 1 hour (intravenous). September 8, non protein nitrogen 32.4; icterus index, 10.2 Patient's appetite was improving though she was still occasionally nauseated and her general strength was somewhat better. She no longer complained of intense weakness and prostration. She was started on thyroxin, grain 1/80, daily. September 16, calcium chloride 5 cubic centimeters of 10 per cent solution was given intravenously and repeated on the next 2 days.

Operation was done September 18. Morphine-atropine preparation; nitrous oxide plus novocain infiltration and block anæsthesia. Through a short, high, right rectus incision the gall bladder was exposed and found to be thick, small, rather red, and completely behind the liver; it was fixed to the upper angle of the wound with Allis clamps and aspirated. A Pezzar catheter was inserted into the gall bladder which was then fastened with Allis clamps to the fascia. Iodoform gauze was packed around the gall bladder and closure was made in layers around the pack and tube; clamps were left in place. Patient was returned to bed with a pulse of 94. After operation there was immediate bile drainage; highest temperature was 100 degrees the first night after operation. The urine output was satisfactory. On September 23, the clamps were removed. On September 26, patient was up in chair and the gauze pack was removed. On October 3, patient was discharged. The incision had healed except for a granulating area immediately around the Pezzar catheter. Bile drainage averaged only 2 to 3 ounces daily.

On October 15, weight was 154 pounds. Two stones passed through the tube. February 11, 1931, three stones were passed. March 15, stools had been normal in color since operation. The Pezzar was changed and lipiodol was injected for visualization of the biliary tree; patient has recently had mild influenza. On May 18, patient was readmitted to hospital; weight was 149 pounds, she having lost 10 pounds since influenza attack. Urine concentration test showed: 6 p.m. to 6 a.m., 410 cubic centimeters; specific gravity, 1,005; 6 a.m. to 9 a.m., 120 cubic centimeters; specific gravity, 1,012. Phenolsulphonephthalein 390

cubic centimeters, 55 per cent in 2 hours (intramuscular); catheter urine was negative; smear of bile showed no pus, numerous gram-negative bacilli, and gram-positive cocci. Lipiodol injection through Pezzar showed obstruction of the common duct and outlined the biliary tree exceptionally well.

Operation was done May 14. Phenobarbital, grains 15, preparation. Nitrous oxide gas and ethylene were used for anæsthesia. Through an incision 2 centimeters to right of the midline everything was found to be adherent to the gall bladder at its junction with the abdominal wall. The ducts were considerably thickened and greatly dilated. Three small pigment stones were removed from the pancreatic portion of the common duct; a probe then entered the duodenum easily. A T-tube was sutured into the hepatic and common ducts and a greatly thickened gall bladder was removed. A Penrose drain was inserted to suture line, brought out with the T-tube through the previous biliary fistula.

After operation, the highest temperature was 101 degrees on the first day; it returned to normal on fourth day. Urine output was good. There was immediate bile drainage of 400 cubic centimeters daily for two days after which it decreased to about 150 cubic centimeters per 24 hours. The stools were of normal color except one passed on the eighth day; patient was quite weak and apathetic for 4 days and was started on thyroxin, grain 1/80, daily. Patient was slow in regaining strength, up on fourteenth day. On June 3, 1931, she was discharged, 20th day. A moderate infection of the drainage tract subsided on irrigations.

July 7, 1931, the stools continued normal in color. We had been clamping off T-tube for past few weeks without symptoms. The T-tube was removed October 30, 1931. No symptoms whatever were noted. July 1, 1932, weight was 168 pounds. Patient eats everything. She has no gastrointestinal symptoms; no pain; bowels move daily; her general health and strength are excellent.

Case 9. Mrs. A. C., aged 62 years, admitted to hospital Jun 27, 1930. For 5 months she had attacks of paroxysmal pain in the right upper quadrant and epigastrium, with vomiting. She was jaundiced during most of the attacks. Her last attack was 3 days before entrance to hospital, with chills and a temperature of 104 degrees. The pain subsided but there was a persistent burning sensation in the region of the gall bladder. Her past history revealed that she had had an operation for "cysts of the ovaries" in 1908 following which the wound burst open and drained for 8 months. The wound reopened and following this she developed an incisional hernia. Operation for ruptured appendix was done in 1923.

Examination revealed a moderate degree of jaundice; heart and lungs negative. The abdominal wall was firm with two old healed incision scars and a small incisional hernia; the right rectus was spastic; there were marked inhibition and tenderness in the right upper quadrant. Temperature, pulse, and respiration were normal. Urinalysis revealed reaction, acid; specific gravity 1,000, occasional white blood cell. She was put on a high carbohydrate intake and fluids were forced. July 1 icterus index was 6.8. July 5, cholecystostomy was performed under nitrous oxide gas plus novocain infiltration and block anæsthesia, after 15 grains of phenobarbital was given by mouth. Through a very short incision a large catheter was sutured into the gall bladder.

The postoperative course was entirely smooth. The catheter came out of gall bladder on the first day after operation and was replaced by a Pezzar (mushroom) catheter. July 10, patient was up in a chair. July 13, she was discharged. July 20, tube came out followed by a small faceted stone. The tube was replaced and continuous drainage instituted. September 26, patient was feeling excellent; eating everything; weighed 120 pounds. October 20, patient reported passing considerable bile at all times through tube, but much more since an attack of headache and a fever of 103 degrees a week previously. Stools were always clay colored; and there was occasional diarrhœa. Sharp epigastric pain was present at times for past few weeks; the appetite was fairly good; she had no chills; weight was 120 pounds. November 12, non-protein nitrogen was 30; icterus index, 5; phenolsulphonephthalein 245 cubic centimeters, 60 per cent in 2 hours (intramuscular). November 15, patient was readmitted to hospital. Blood pressure was 130/78. The liver was not palpable. A Pezzar catheter was placed in the fistula. The stools were usually acholic. She had been fed bile salts continuously since previous discharge. She started on thyroxin, grain 1/80, daily. Catheter urine showed reaction, acid; specific gravity, 1,015; microscopically and chemically negative.

Operation was done November 18. Phanadorn, grains 15, preparation was carried out. Nitrous oxide anæsthesia was used. Through an incision, high in the right rectus and close to midline, the gall bladder appeared little changed; no stones were found in the gall bladder or cystic duct; the common and hepatic ducts enormously dilated, with walls gray and thick; the common duct contained multiple pigment stones in its entire pancreatic portion. The stones were removed and the instruments readily passed into the duodenum. A large catheter was sewed into the hepatic duct; a Penrose to suture line in common duct; the wound was closed. Pulse was 78 at end of operation. The highest temperature after operation was 101 degrees on first night; normal after fourth day. Urinary output was good at all times. Bile drainage was immediate and averaged about 200 cubic centimeters for 24 hours, until the catheter came out of the hepatic duct on the eighth day after operation. Drainage through the Pezzar catheter in the gall bladder was thereafter only about 75 cubic centimeters per 24 hours. December 1, up in chair. December 6, discharged with incision completely healed. There was no bile drainage around the Pezzar catheter. The Pezzar catheter was removed in March, 1931, after lipiodol injection had shown the common duct to be patent and emptying promptly into the duodenum. The fistula healed in about 10 days. May 19, 1931, patient weighed 128 pounds and excellent in every way. June 28, 1932, weight, 143, digestion excellent, bowels moved daily without cathartic, eats everything; blood pressure 145/75; considers herself 100 per cent normal.

Case 10. Mrs. O. D., aged 49 years, was admitted to hospital July 26, 1930. For past 3½ years she had had sensation of distention of abdomen and belching after meals, particularly after eating fat; occasional stabbing pain in right upper quadrant during this time. She had had intermittent pain during past month; no jaundice; stools of normal color.

Examination revealed the following: heart size cannot be made out, sounds regular, only fair quality; blood pressure 144/78; lungs negative; abdomen: much fat; considerable spasm; tenderness and inhibition in right upper quadrant; lower quadrants negative; pelvis and rectum normal; weight 163 pounds. Voided urine was alkaline, specific gravity 1,003, a few white blood cells and bacteria.

Operation was done July 29. Phenobarbital, grains 15, was given in divided doses as preparatory measure. Spinal anæsthesia was used. Through a high right rectus incision a long, adherent, scarred appendix was removed. The gall bladder was found to be thick, gray, incompressible,

and filled with black bile, much mucus, and sand. Patient's condition on the table became unsatisfactory and it was thought unwise to perform cholecystectomy. Drainage of the gall bladder was therefore carried out with a Pezzar catheter.

Temperature went to 103 degrees on night of operation and to 103.4 degrees the following night, gradually returned to normal but rose to 99.4 degrees almost daily for 2 weeks. The incision healed cleanly. Patient allowed up on twelfth postoperative day. September 16, she was discharged, weighing 145 pounds.

The subsequent course has been uneventful. February 11, 1931, she reported her digestion vastly improved; no pain or belching and sensation of fullness rare, but drainage was averaging 5 ounces per 24 hours. She was instructed to clamp off the catheter continuously as long as no discomfort resulted. In July, 1931, she described her condition as perfect and removal of the gall bladder was advised. January 6, 1932, she reported her digestion excellent, weight 168 pounds. She had been wearing the tube clamped off continuously for 6 months without symptoms. She was still deferring operation because of inability to meet hospital expenses and was to continue wearing the tube until she could arrange to re-enter the hospital for cholecystectomy.

Case 11. Dr. F. S., aged 64 years, was admitted to hospital September 4, 1929. He had had a posterior gastroenterostomy in 1914 for duodenal ulcer with relief of pain, but persistence of occasional attacks of nausea were relieved by induced vomiting of large amounts of bile-stained fluid. Ten years ago he began having mild attacks of pain in the right upper quadrant with nausea and vomiting followed by tenderness in the upper abdomen for about a week. Attacks were precipitated by eating sweets, meat, or fried foods. One week ago he had a very severe attack of pain in the right upper quadrant and back and to relieve pain induced vomiting and took morphine. Temperature 102 degrees; he had no chills or jaundice; no abnormal stools.

Examination revealed weight, 142 pounds. The head, neck, and chest were essentially normal for his age. There was a rather marked thickening of the peripheral vessels; blood pressure was 130/86. The right upper quadrant was tender; the liver was palpable one to two finger breadths below the right costal margin; the edge was sharp and tender; there was marked positive inhibition. There was an old healed midline scar. Temperature was 99.6 degrees; pulse, 90; respiration, 22; white blood cells, 10,000; red blood cells 3,800,000; hæmoglobin 85 per cent; van den Bergh, negative; icterus index, 4.8; non-protein nitrogen, 25. Urine on September 6, acid, specific gravity, 1020, microscopically and chemically negative. A transfusion of 500 cubic centimeters citrated blood was administered and patient was discharged on September 11, because of head cold which had been hanging on for several days. He was readmitted September 18 and he was operated upon the following day.

Phenobarbital, grains 12, were given as a preliminary measure. Nitrous oxide gas plus novocain infiltration and block anæsthesia were used. A large non-faceted pigment stone was removed from the gall bladder, the mucosa of which was grossly necrotic; the gall bladder was stuffed with a small iodoform pack in the hope of obliterating it. All ducts were grossly normal and were not explored. Patient vomited considerably and hiccoughed for the first 3 days after operation. His highest temperature was 101 degrees, he sweated profusely, and had very obviously had all the operating that he could have withstood. The course thereafter was smooth. The gauze was removed from the gall bladder. A Pezzar catheter was inserted in its place, and the patient discharged on October 3, with the incision healed.

The Pezzar came out in about a week after discharge from the hospital and was not replaced. The fistula healed in 10 days. November, 1930, his weight was 157 pounds. September, 1931, his weight was 153 pounds; July, 1932, his weight was 151. Patient has been working continuously as a general practitioner since 6 weeks after discharge from the hospital. About every 3 months he has an attack of mild pain in the right upper quadrant with nausea, both of which are relieved by lavaging his own stomach from which he recovers large quantities of bile-tinged fluid. He can still precipitate such attacks by eating too much meat, eggs, chocolate or milk, or by getting quite tired. These attacks do not incapacitate him. He enjoys complete comfort otherwise and his strength is good. He considers himself 75 per cent normal.

Case 12. Mr. J. F., aged 70 years, was admitted to the hospital, September 17, 1930. He had had intermittent pain in the left upper quadrant and epigastrium for past 6 months without other symptoms. Five days ago he had begun to vomit almost everything he ate and had had a constant gnawing pain in the epigastrium. He had daily passage of normal stool; no jaundice.

Examination revealed a weak, exhausted elderly man in moderate pain. The head, neck, heart, and lungs were normal for his age; no obvious dehydration. The abdomen was very tender in the right upper quadrant. There was marked inhibition on respiration. The epigastrium was less tender. The lower quadrants were negative. The genitalia and rectum were normal. The extremities were negative except for a rather marked thickening of the peripheral vessels. Temperature was 97.2 degrees, pulse, 84; respiration, 20; blood pressure, 120/80, differential (Schilling) count, infectious type; urine, acid, two plus albumin, numerous hyaline and granular casts, a few white blood cells.

Patient vomited at intervals for the first 4 days but was thereafter perfectly comfortable; temperature remained normal. September 19, non-protein nitrogen was 64.5; phenolsulphonephthalein no trace 1 hour (intramuscular). Test meal showed no free hydrochloric acid, positive for bile, negative for occult blood. Stools were of normal color and negative for blood. Gastro-intestinal and gall-bladder series of films revealed a deformed gall bladder shadow with some pulling of the second portion of the duodenum toward the right. September 22, phenolsulphonephthalein 345 cubic centimeters, 24 per cent in 2 hours (intramuscular). Urinalysis showed specific gravity 1,005, microscopically a few organisms. September 29, phenolsulphonephthalein, 375 cubic centimeters, 47.5 per cent in 2 hours (intravenous). Amount of urinary output during this pre-operative course was not recorded.

Operation was done October 3. Nitrous oxide gas, ethylene, plus novocain infiltration and block anæsthesia were used. The gall bladder was incompressible and adherent to the duodenum by extensive adhesions; the pylorus bound down but normal on palpation and inspection. Cholecystostomy was performed by the usual technique; drainage was carried out with a Pezzar catheter.

The postoperative course was entirely smooth and on October 13, patient was discharged. A report from his referring physician at the present time states that the patient wore the tube 8 months; had no pain, but occasional belching after meals; regained normal strength and weight. At the end of 8 months the tube broke off at the level of the skin and he entered another hospital as a clinic patient where the tube was removed and cholecystectomy was performed because it was felt that the gall bladder was non-functioning. His present health is said to be good.

CASE 13. Mr. H. Y., aged 53 years, was admitted to the hospital January 24, 1930. He complained that 20 years ago for a period of about 6 months he suffered fullness and dull discomfort in the right upper quadrant after eating meat or fried foods. He eliminated these foods from his diet and enjoyed fair comfort until 8 years ago when pain recurred and he was slightly jaundiced for 2 or 3 months and had clay colored stools. Indigestion persisted until 6 months ago when agonizing pain recurred with nausea and vomiting during which a left inguinal hernia appeared. Intermittent pain and great eructation had been present since this attack. His best weight was 130 pounds, fifteen years ago. His average weight is 125 to 128; present weight, 115 pounds.

Examination revealed a small, thin man looking older than his years; skin and sclera clear; mouth foul; heart and lungs normal; blood pressure 120/70. The abdominal muscles were very lax and there was an obvious bulge in the right upper quadrant representing the liver, which extended from the sixth intercostal space in the right midclavicular line to four finger breadths below the costal margin, edge rounded, quite tender. The gall bladder was not palpable. The lower quadrants were negative. The extremities were negative. The temperature, pulse, and respiration were normal; blood and urine normal; stools, normal, negative for occult blood. Phenolsulphonephthalein output was 340 cubic centimeters, 85 per cent in 1 hour (intravenous); electrocardiagrams showed ventricular extrasystoles and left axis deviation. Gastro-intestinal X-rays showed the second portion of the duodenum pulled to the median line; the stomach emptying promptly and a redundant colon lying largely in the pelvis. He was given blood transfusion and 10 cubic centimeters 10 per cent calcium chloride intravenously on 2 successive days before operation. Pre-operative diagnosis was chronic cholecystitis and chronic choledochitis, question biliary cirrhosis.

Operation was done in January, 1931. Phenobarbital, grains 15, were given in preparation. Ethylene anæsthesia was used. Through a right rectus incision the right lobe of the liver presented a rounded border of finely granular surface, grayish-red in color, no gross nodules. On the peritoneal surface of the ascending colon were several firm yellow nodules the size of BB shot, one of which was removed for biopsy. The gall bladder was enormously dilated, not adherent, thin walled, and incompressible. The pyloric end of the stump and transverse colon were attached firmly to the region of the common duct which could not be readily palpated. The spleen was smooth, somewhat enlarged. The gall bladder was aspirated of greenish, normal appearing bile and then a large soft rubber tube was inserted into it and transfixed. A small wedge was taken from the liver edge for biopsy. A drainage tube was clamped for gradual decompression. The wound was closed about the tube. Pathological report of the nodule from the colon was vegetable fiber stalk with foreign body reaction and fibrous connective tissue encasing it. The section of liver showed moderate degree of pigmentation and low grade chronic inflammation and infiltration. Diagnosis: low grade chronic hepatitis.

Patient was returned to room with pulse 84. Decompression of the gall bladder was carried out by releasing 1 ounce of bile from the tube every hour for the first 24 hours. Continuous drainage was then allowed. The highest temperature was 101 degrees on first day after operation. It was normal after the fourth day. The patient, however, was extremely weak and we felt assured that more radical operation would probably have proved fatal. For the first 2 weeks, bile drainage varied from 450 to 1,200 cubic centimeters per 24 hours, averaging about 700 cubic centimeters. Bile salts were fed by mouth and the patient's condition gradually improved. On the tenth postoperative day he was given another blood transfusion; on the twelfth day he was allowed up; on the fifteenth day the tube came out of the gall bladder and was replaced with a Pezzar catheter and the bile drainage was less than 500 cubic centimeters per 24 hours at all times. February 22 he was discharged with instructions to replace all bile drainage as retention enema when it amounted to more than 200 cubic centimeters per 24 hours.

The Pezzar came out one month later and as the drainage had greatly diminished in amount and stools had been of normal color at all times it was not replaced. The fistula closed in 10 days. July 5, 1932, patient returned weighing 125 pounds, having had perfect digestion ever since operation; no pain or jaundice; no sensation of fullness or belching; liver edge still nearly to umbilicus, but edge is sharp and upper border at sixth rib by percussion and is apparently only ptosed rather than enlarged now. Patient has urinary symptoms with 2.5 ounces residual urine because of a small fibrous prostate which will probably require a cautery punch. Following elimination of this source of straining we will repair his inguinal hernia.

SUMMARIES OF CASES

1. A patient aged 57 years, recently jaundiced, had suppression of urine, nitrogen retention, hypertension, positive urine of low specific gravity, no œdema but marked diuresis, on recovery. At second admission, following cholecystostomy, the urine was of higher specific gravity, hypertension was improved. Cholecystectomy was done. Patient now has developed diabetes mellitus, toxic adenoma of thyroid, hypertension is still present; gastro-intestinal status is excellent.

2. Patient aged 58 years, jaundiced, had suppression of urine, nitrogen retention, increasing blood pressure, positive urine of low specific gravity, œdema. She died without operation. Gross autopsy only was done.

3. Patient aged 71 years, jaundiced, had 42 per cent retention of iso-iodekon in 30 minutes (liver failure) on admission, suppression, nitrogen retention after partial diuresis, positive urine of low specific gravity, œdema, low blood pressure, slow pulse. Patient died without operation. Autopsy showed characteristic kidney lesions.

4. Patient aged 53 years, jaundiced, was known to have had normal urine and normal phenolsulphonephthalein output 1 month before; suppression, nitrogen retention, œdema. Urinalysis was not reported. Patient died without operation. No autopsy.

5. Patient aged 61 years, jaundiced, showed positive urine of moderate specific gravity on entrance and slight nitrogen retention 3 days later. Jaundice subsided. One week after cholecystectomy and exploration, common duct developed moderate suppression, nitrogen retention, positive urine, simultaneous with blocking internal bile drainage, cause unknown, and deepening jaundice. Death occurred and no autopsy was obtained.

6. Patient aged 63 years, had never been jaundiced. On admission to hospital with empyema of gall bladder she showed suppression, no nitrogen retention, positive urine, slight hypertension. No function tests were recorded. The output rose after operation. Cholecystostomy was done. Convalescence was normal until he died suddenly from pneumonia on eleventh day. No autopsy was made.

7. Patient aged 37 years, recently jaundiced. Urine was normal and of rather low specific gravity (1,014 highest recorded) and decreasing phenolsulphonephthalein output (37.5 per cent) on first admission. Cholecystostomy was done. The phenolsulphonephthalein output increased to 53 per cent. Cholecystectomy was done after

lipiodol injections showed patent common duct. Present status revealed definite hypertension (155/95) only partly due to toxic thyroid.

8. Patient aged 64 years, had had a subsiding jaundice of recent origin, with urine practically normal, no nitrogen retention, good phenolsulphonephthalein output. Graded operation was chosen because of the age and general weakness of patient since exploration of common duct was indicated. Cholecystostomy was done. On second admission, lipiodol injection was done through a Pezzar catheter and showed a block of the common duct and little alteration in the hepatic tree. Cholecystectomy and choledochostomy (T-tube) were withstood. Check-up lipiodol injection through T-tube showed patent common duct before removal of tube. Present status is excellent.

9. Patient aged 63 years, had very slight subsiding jaundice. The findings were very similar to those in Case 8. Graded operation was done because of weakness and age. Patient lost 25 pounds in weight. Exploration of common duct was indicated. Cholecystostomy was done. Patient was discharged and readmitted for choledochostomy which was well withstood. Present status is excellent.

10. Patient aged 49 years, never had been jaundiced, urine was normal, no functional test recorded. Stage operation was not planned. Condition became poor on table after only appendectomy. Present status is excellent. She is still wearing Pezzar catheter. Cholecystectomy is still to be done.

11. Patient aged 64 years, had never been jaundiced. The urine was normal, there was no nitrogen retention, but a moderate anæmia. Patient had marked arteriosclerosis; he seemed "older than his years." Cholecystostomy was planned and performed. He could not have withstood more. Present status is 75 per cent normal.

12. Patient aged 70, had never been jaundiced. He was admitted to hospital in acute attack of cholecystitis, phenolsulphonephthalein output was not recorded, there was nitrogen retention. Urine was positive, no phenolsulphonephthalein excretion at first test. Function improved as attack subsided. Permanent cholecystostomy was advised because of his age and so severe an illness. We do not approve of his reoperation elsewhere.

13. Patient aged 53 years, was jaundiced in the past. His urine was normal, function good. He was thin and run-down. With gross liver changes present at operation and old, extensive adhesions around common duct, it was thought unwise to proceed beyond cholecystostomy. This was borne out by his course in the hospital. Present status is excellent.

Cases 14 and 15 are mentioned merely because the lipiodol injection through T-tubes in their common ducts illustrate so well the value of this method of outlining the biliary tree. The dilatation of the intrahepatic radicals shows clearly, persisting 10 months after plastic operation for stricture in Case 14. The film of Case 15, taken 12 days after choledochostomy, shows the same dilatation and prompt emptying of the ducts. If it is desired to outline the biliary radicals in the liver, injection through Pezzar catheter in the gall bladder or through the T-tube in the common duct should be made with the patient in the Trendelenburg position under the fluoroscope. We had been making such observations for about a year before the publication of Overholt's preliminary report. The plan is very useful; it is a real addition to our means of following patients with therapeutic biliary fistula. We hope to see the dilatation of the intrahepatic radicals disappear in Case 15 before we remove the T-tube, for this would be the best evidence of restitution of normal anatomical status. When we have been able to follow with lipiodol injection the course of a larger group now under observation, Dr. John Young and the author propose to publish the results in full.

Excluding Case 5, which occurred previous to the start of this study, 56 patients with diseases of the biliary tract have come under our care. Operation was not performed in 3 (Cases 2, 3, 4). On the remaining 53 patients primary cholecystectomy was performed in 37 cases with exploration of the common duct in 2. There were 2 deaths in this group, both of overwhelming pneumonia and septicæmia, one occurring on the sixth, the other on the eighth postoperative day, in women under 40 years; both occurred previous to the adoption of carbon dioxide inhalations as routine postoperative care. Cholecystostomy was done as the first step of a contemplated graded operation in 6 patients (Cases 1, 6, 7, 8, 9, 10), followed by subsequent cholecystectomy in 2 (Cases 1, 7), by exploration of the common duct with cholecystectomy in Case 8 and without cholecystectomy in Case 9. Case 10 has not yet had her final operation. The one death in this group occurred in Case 6, pneumonia developing on the fourteenth day after a reasonably smooth postoperative course. Cholecystostomy as the only contemplated operation was performed in 5 patients, among whom are Cases 9, 12, and 13; temporary drainage of the gall bladder was instituted in 2 other patients, one being a woman operated on with a diagnosis of perforating ectopic pregnancy and found to have acute appendicitis and a gall bladder full of calculi; the other a man on whom appendectomy was performed in an interval of intermittent appendicitis, the gall bladder being somewhat thickened, without stones, but high under the liver and very difficult to reach. Secondary cholecystectomy was performed on 2 patients, one of whom had had a stone left in the cystic duct following cholecystostomy elsewhere 6 months previously; we had performed cholecystostomy on the other patient 9 years previously. In the 3 remaining cases exploration of the common duct for stricture in one case and for stone in the other 2 was performed. The patient with stricture and one of those with stone were jaundiced at the time of operation; they were the only cases of

all the jaundiced patients that bled after operation in spite of the usual preparation with calcium chloride and transfusion of blood.

Until recently there was no clinically useful dye test for liver function. With the introduction of iso-iodekon, such a test seems at hand. We do not look for any great reduction in postoperative mortality from its use in our own practice, for it is obvious that we have not been operating upon patients with badly failing livers. We feel that wider appreciation of the need for thorough evaluation, particularly from the standpoint of the renal anatomical and physiological status, of all patients with biliary tract disease will be more generally effective in reducing operative mortality. Renal insufficiency occurs in such patients in the absence of jaundice, especially in patients in an acute exacerbation. The occurrence of nephritis in them must be laid to infection, and a study of the infecting organism in such cases is especially indicated. *Acute nephritis is uncommon in other diseases of the abdominal viscera amenable to surgical attack.* It is a fact that operations on only the biliary tract are done for chronic intra-abdominal infections, with the exception of those on the female pelvis in whom conditions for absorption, localization, and drainage are quite different. (We see little clinical or pathological evidence for the existence of chronic appendiceal infection unmarked by exacerbations recognizable as acute attacks.) We believe that for this reason an unbearable burden is thrown on the kidneys more often in operations on the biliary tract than elsewhere. The point can be forced to an extreme by considering how often nephritis and anuria would occur if patients with scarlatina were given an ether anæsthesia lasting for an hour and subjected to a major operation!

Simply because the barbituric acid compounds are excreted largely through the kidneys, we do not propose to use them as pre-anæsthetic preparation for this group of patients in the future. Where a stage operation has been decided upon, paraldehyde, or some other drug excreted through the lungs, can be given by rectum before taking the patient to the operating room. A light nitrous oxide or ethylene anæsthesia should be used to mask the infiltration and blocking of the abdominal wall. Cholecystostomy can then be performed by the technique outlined in the case histories in less than 15 minutes, ordinarily. If an inhalation anæsthetic is required, ethylene is preferable to nitrous oxide since any degree of cyanosis threatens all cellular metabolism. Morphine should be used very sparingly for the same reason.

CONCLUSIONS

1. A review of the literature on renal complications of biliary tract disease is given.

2. Six cases of nephritis with suppression of urine complicating biliary tract infections are presented. To these a seventh (Case 12) should probably be added. With one exception (Case 5) these occurred in a series of 56 consecutive patients, an incidence of 10.7 per cent.

3. This complication occurs at times, particularly in acute exacerbations, without jaundice and can be detected in its incipiency. Functional tests are discussed.

4. Excretion of phenolsulphonephthalein in patients in whom primary cholecystectomy or choledochostomy was performed has varied only within the normal range for the age of the individual.

5. There is no evidence that hepatic cell damage serious enough to cause liver failure must precede renal damage, though ordinarily the two are associated.

6. Stage operations are advocated for patients who have suffered from renal complication, as well as for all seriously depleted patients with biliary tract disease. Illustrative cases are presented in which cholecystostomy is done as a preliminary step and others in which it is the only operation contemplated.

NOTE.—Since this paper was submitted for publication, an article by Helwig and Schutz has appeared, which deserves comment. They regard nephritis as secondary to degeneration of liver tissue, as did some of the early German authors. They correctly note the inconstancy of jaundice as an etiological factor. However, their observations and conclusions may be adversely criticized on the following points: (1) They disregard the evidence of active infection in Cases 1, 3, 5, and 6 (exacerbation of symptoms before operation and acute inflammation found at operation) as unimportant in precipitating postoperative renal failure. (2) They describe laboratory findings as being "normal" before operation, which raises the suspicion that a blood non-protein nitrogen determination within normal limits was accepted as evidence of normal kidneys. (3) Their experimental work consisted in producing a limited necrosis of the liver by trauma. The production of acute nephritis by liberation of products of aseptic necrosis of other tissues (as in skin burns and in acute pancreatitis with fat necrosis) is well known; their experiments are not evidence for specific action of liver necrosis on the kidney parenchyma. (4) They characterize the condition under discussion as "hepato-renal syndrome" which obscures the clear-cut evidence that acute nephritis following infections in the bile passages or destruction of liver tissue (just as after infection in the throat) occurs more frequently than has been previously thought. The statement that the "syndrome" has been previously undescribed is hardly warranted, in view of the literature which they, as well as I, have summarized.

I am satisfied that we are both describing the same clinical condition; they disregard the rôle of infection in the bile passages as being the direct cause of the nephritis

while I consider it of the greatest etiological importance and believe that a specificity for renal tissue of the toxins of the infecting organisms will eventually be shown.

A recent communication by Ginzburg calls to my attention a previous publication of lipiodol injections through biliary fistulæ with very satisfactory results.

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EDITORIALS

SURGERY, GYNECOLOGY AND OBSTETRICS

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JUNE, 1933

THE CENTURY OF PROGRESS

FUR Trading, Indians, French, Wars, Missionaries, Cholera, Fort Dearborn, The United States Army, Emigration from the East, Fort Dearborn Massacre, Rail-Splitting, Primitive Medicine and Midwifery, War Wounds, Vision, Courage, Faith, Perseverance, Foundation of Medical Schools and Societies, Success. Such are the chapter headings of the history of Chicago and its environs of a century or so ago.

During the intervening years Chicago has run the gamut of the helps and hindrances of civilization. Its strategic geographic situation and the character of its citizenry have drawn to it everything that goes to make up a metropolitan center of cosmopolitan interests and to establish it as an epitome of world progress.

Forty years ago in Chicago the discovery of America was memorialized by the Columbian Exposition, the world's fair after which subsequent world's fairs have been patterned. This year the centennial of Chicago will be memorialized by a Century of Progress, a new type of world's fair in which the nations will co-operate to display the present scientific, religious, and artistic status of the world.

From June 1 to November 1 the beautiful lake front of Chicago will present the forefront of the march of progress in achievement. The very inventions and discoveries of the Century which have brought about the present mechanical age have made it possible to make the displays in a way that was heretofore impossible.

The science and art of the engineering profession have produced changed conditions of life, and the science and art of the medical profession have made life safer, better, and longer under these new conditions.

The products of the basic sciences of chemistry and physics as exemplified in the conversion of raw materials into articles of utilitarian and artistic value will be exemplified, and the leading spirits of the exposition have set a new tempo by emphasis on a display of the processes of manufacture as well as on the finished products.

The use of steam, oil, gasoline, and electricity in the production of light, heat, and power, and the application of these to mining, agriculture and manufacture, transportation, communication and illumination, are products of this last century and so will occupy important places in the exposition.

The artistic side will be interwoven in all phases of the Fair by a new use of color, light, architecture, sculpture, and painting.

Of particular interest to the medical profession will be the exhibits on the medical and biological sciences which will receive a prominence not hitherto accorded them in such general expositions. Universities, national,

state, and civic medical institutions and commercial organizations will vie with one another, and the result cannot but be reflected in a better comprehension of medical and surgical problems by the public. From this will come improved health of the people through a better and surer knowledge of how disease is caused, prevented, and cared for, and how these benefits may be derived from the medical profession.

The American Medical Association, the American Dental Association, the Wellcome Research Institution, the American College of Surgeons, a number of our universities and large private medical clinics have prepared attractive and instructive exhibits. The following is a brief summary of the exhibit of the American College of Surgeons:

Improvements in surgery in America during the past century will be portrayed by five beautifully executed dioramas. Details of hospitals and their care of the sick and injured, during the nineteenth century and today, will be depicted by transparencies, models, a semi-diorama, and an illustrated map. A replica of the Lister exhibit in the Wellcome Historical Medical Museum. SURGERY, GYNECOLOGY AND OBSTETRICS, the official journal of the College, will exhibit an authentic record of surgical progress. The College activities, surgical progress, and service to the public will be described through illustrated lectures. The objects and activities of the College will be further illustrated by illuminated wall plaques. The exhibit will be enhanced by the use of portraits of eminent American surgeons of the century, the Great Mace of the College, the Seal of the College in magnified form, and by other means.

During the period of the Century of Progress, Chicago will be host at the annual meetings to a number of the national medical organizations.

ALLEN B. KANAVEL.

SUBPHRENIC INFECTIONS

UNFORTUNATELY, the importance of subphrenic infections is not sufficiently appreciated by most surgeons. The majority of subphrenic infections are the result of an intra-abdominal contamination, usually caused by extension of micro-organisms from an abdominal viscus. Rarely subphrenic infections may extend from extra-abdominal foci either by direct extension (from the thorax) or through the blood stream. Only a relatively small percentage of subphrenic infections proceed to abscess formation. By far the larger number resolve spontaneously which probably accounts for the fact that subphrenic infections without abscess are relatively infrequently diagnosed. The most frequent cause of subphrenic infection is post-appendiceal peritonitis. However, in all cases of acute peritonitis the possibility of the development of a subphrenic infection must be kept in mind, as in this way the early diagnosis is facilitated. Subphrenic infections following acute appendicitis characteristically are found most frequently in the right posterior superior space, viz., above the liver on the right side and behind the right prolongation of the coronary ligament. This infection is manifest clinically by a persistent point of tenderness over the right twelfth rib. An infection inferior to the liver, but on the right side, i.e., right inferior space infection, may occur concomitantly with right posterior superior infections.

The prognosis in subphrenic infections is very good because only relatively few of the infections progress to suppuration. The prognosis in subphrenic abscess has been considered as being especially grave, due to two facts: (1) the diagnosis of the infection is made relatively late, and (2) most subphrenic abscesses have been drained either transpleurally

or transperitoneally and because of contamination and subsequent infection of one of the large serous cavities (the pleural or peritoneal) an overwhelming and fatal toxæmia develops. The mortailty rate in collected series of cases varies from 20 to 100 per cent. In the treatment of subphrenic abscess the same surgical principles as used elsewhere in the body should be applied. Whereas it is frequently possible to drain an intraperitoneal abscess through an uninvolved peritoneum by attempting to protect the virgin peritoneum from contamination, it is far better to drain the abscess extraperitoneally as the danger of contamination of the peritoneum is thus obviated. Similarly, it is far better to drain subphrenic abscesses extraperitoneally in such a way that contamination of the pleural and peritoneal cavities is prevented. In abscesses pointing anteriorly, extraperitoneal approach is possible by reflecting the peritoneum from the under surface of the diaphragm until the abscess is encountered. In those abscesses pointing posteriorly the retroperitoneal operation (2) permits adequate exposure and drainage of abscesses in this region without the danger of contaminating either the peritoneal or pleural cavity. The advantage of the extraperitoneal operations over the other methods of approach is exemplified by Flynn's (1) statistics of cases of subphrenic abscess operated upon by members of the Southern Surgical Association. In those cases in which operation was by the transpleural, transperitoneal, or extraperitoneal method, the mortality rate was 37.9 per cent; in those cases in which operation was by transpleural or transperitoneal routes the mortality rate was 41 per cent; whereas in those cases in which operation was by the extraperitoneal technique the mortality rate was 18.4 per cent. In 19 personal cases operation was by the retroperitoneal operation and there was but one death, a mortality rate of 5.2 per cent (3). In fact, it is my firm belief that subphrenic abscesses should be treated successfully with no mortality. This can be accomplished, however, only by the early recognition of the condition and the institution of adequate drainage without contaminating uninvolved serous cavities. ALTON OCHSNER.

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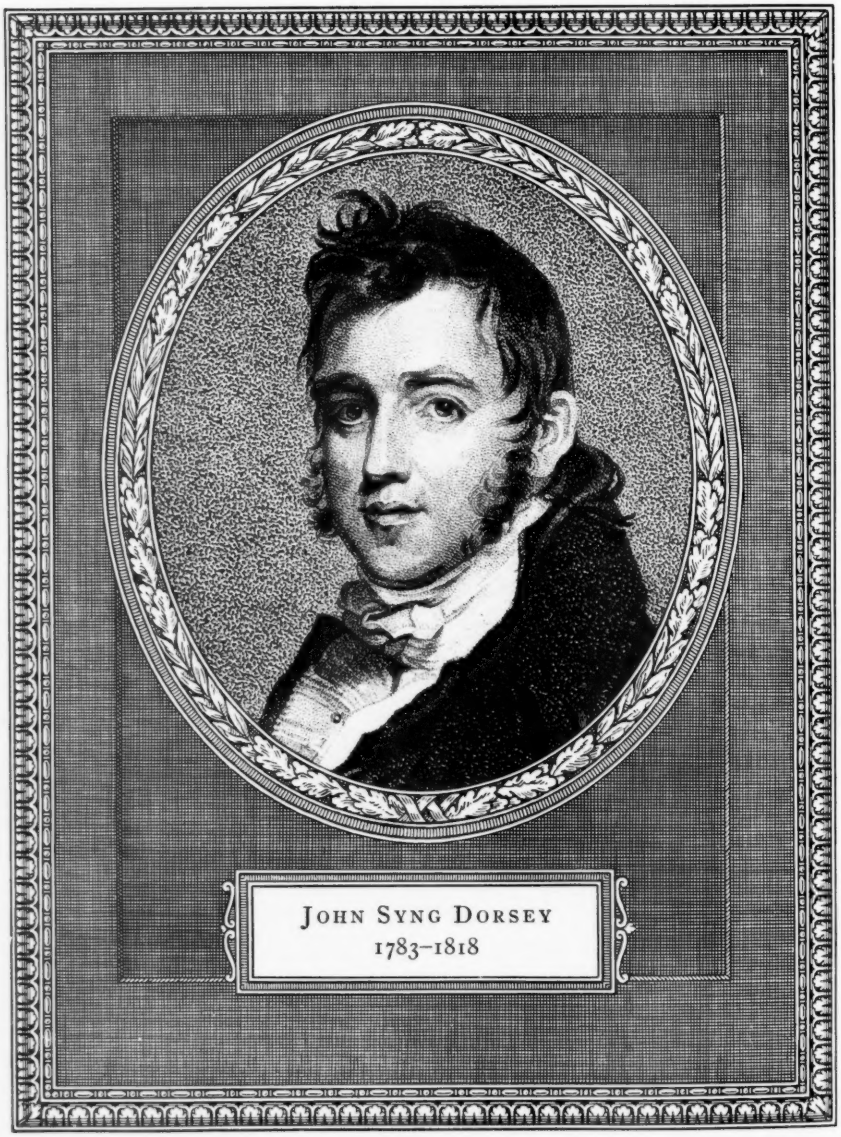

JOHN SYNG DORSEY
1783–1818

UNIV. OF MICH.

MASTER SURGEONS OF AMERICA

JOHN SYNG DORSEY

FROM time to time in history there have lived men who have been able to accomplish a full life's work within a brief span of years. A man of this mold, John Syng Dorsey, was able during his thirty-five years of life to reach a prominent place in American surgery of the early nineteenth century. Like his contemporary the great composer Franz Schubert, who lived but thirty-one years, he seemed unconsciously to sense the need for filling every moment so that his successive achievements came with dramatic frequency.

Members of the old English family of D'Orsey were early settlers in Maryland, but John was born in Philadelphia in 1783 where his father, Leonard Dorsey, was a prominent merchant. Young Dorsey passed rapidly through his classical studies at the Friends' Academy and the University of Pennsylvania, overcoming the handicap of a slight defect in speech and graduating with distinction at the age of fifteen years. He began at once the study of medicine at the University of Pennsylvania under the guidance of his noted uncle, Dr. Philip Syng Physick, who held the chair of surgery at that time. A year prior to his graduation he was honored with a membership in the Medical Society of Philadelphia; Benjamin Rush was then president of the organization. In that same year Dorsey became a member of the Chemical Society of Philadelphia, an organization "desirous of promoting the cultivation of the science of chemistry in the United States of America by associating with themselves persons of distinguished talents." In 1802, at nineteen years of age, he defended his thesis on "The Powers of the Gastric Juice as a Solvent for Urinary Calculi" and received his degree of Doctor of Medicine; a special dispensation from the board of trustees waived the requirement that candidates for the degree must be twenty-one years of age.

Coincident with his graduation occurred one of the severest epidemics of yellow fever in the history of Philadelphia, and young Dr. Dorsey was made resident physician of one of the emergency hospitals. During his year of service there he demonstrated his sincere faith in his own reasoning and convictions. He believed with Deveze that yellow fever was not contagious and fearlessly went about the care of his patients, constantly exposing himself to the disease, whereas many of his confrères who entertained similar ideas were unwilling to vindicate them.

In 1803 Dorsey sailed to Europe for a year of study. The entire winter was spent in London where he attended the lectures of the famous chemist, Sir Humphry Davy, but spent the most of his time in John Hunter's anatomical school where in former years his uncle, Dr. Physick, had so distinguished and endeared himself that the great anatomist had made an offer of partnership. Dorsey spent the remaining portion of the year in Paris where he continued his studies in anatomy.

In 1804 Dorsey returned to Philadelphia and prepared to practice his profession. Those first few years must have carried all of the traditional monetary anxiety, for his old account books reveal that his income for the first year was only $325.75. However, appreciation of his ability spread steadily and in a few years he was considered one of the most skillful surgeons in the country. He was elected to the staff of the Pennsylvania Hospital where the first ligation of the external iliac artery for aneurism was performed by him. It was during this period that he prepared the manuscripts for his great book, "Elements of Surgery," a work which received much recognition and was reprinted in Edinburgh as a textbook for the university. The material it contained was drawn partly from his own experience but largely from the experience of his uncle, Dr. Physick, to whom the book was really a monument, for Dr. Physick left but few writings of his own. Dorsey's talent and training as a draughtsman enabled him to prepare his own beautiful illustrations.

At the age of thirty-two, Dorsey accepted the chair of materia medica in the University of Pennsylvania and soon endeared himself to his pupils by his tireless interest in their work and the frank, sympathetic manner of his teaching. Following the example of Wistar, he valued and thoroughly enjoyed informal gatherings with his students where exciting controversies often developed, stimulated by his clear, direct thinking and youthful enthusiasm. He loved to debate and his discussions at medical meetings always attracted interest, often were at variance with current opinion, but never were injured by petty meanness or personal rancor. His association with great men abroad and his great love for music and poetry mellowed the brilliance of his scientific fervor and made his character of outstanding appeal.

In 1818 occurred the sudden death of Dr. Caspar Wistar, the highly respected and much loved professor of anatomy at the University of Pennsylvania. It was he who had first developed in this country the continental plan of informal discussions between professor and students, and it was through his efforts over a long period of years that the teaching of anatomy had reached such a high plane there. John Dorsey was selected to fill the vacant chair, a difficult task but one which he accepted with sincere confidence and reverent respect for his predecessor. On November 12, 1818, he delivered the introductory lecture to his students. It was an inspiring talk of outstanding richness of thought, carefully designed to lead the

beginners in medicine beyond the unfamiliar horrors of the dissecting room to an earlier realization of the value of true knowledge and a visualization of the long vista of interesting work before them. "No oratorical displays of rhetoric or eloquence can aid the anatomist to enliven your attention," he told them, "his eloquence is of the hand; his rhetoric of the scalpel! But when the years shall have rolled away and your memory shall be tasked to recall the vestiges of scholastic learning, when your teacher's tongue shall be silent and his hand motionless, then the impressions derived through the medium of your senses will be found fresh and vivid long after the collections of impassioned oratory shall have faded from your minds."

The tragic drama of this counsel was to be realized with terrible suddenness. Within a few hours after this, Dorsey's first address to his class, he was stricken with a fatal illness which proved to be typhus fever. He died ten days later, thus ending at thirty-five years a career of such achievement as to rank him among the foremost surgeons of his time, and of such promise that inevitably he would have been grouped with the great men of all time. LEONARD FREEMAN, JR.

CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

J. BENTLEY SQUIER, New York, *President* WILLIAM D. HAGGARD, Nashville, *President-Elect*

FRANKLIN H. MARTIN, Chicago, *Director-General*

PHILIP H. KREUSCHER, *Chairman;* OSCAR E. NADEAU, *Secretary, Committee on Arrangements*

PLANS FOR THE 1933 CLINICAL CONGRESS IN CHICAGO

FOR the twenty-third annual Clinical Congress of the American College of Surgeons, to be held in Chicago, October 9–13, 1933, the surgeons of that great medical center are keenly interested and have organized to provide for the Fellows of the College and their guests, a program of surgical clinics and demonstrations that will present a most complete showing of the city's clinical activities in all departments of surgery. In these plans the Committee on Arrangements has been assured of the hearty co-operation of the surgeons of the four medical schools and more than fifty hospitals that will participate in the clinical program.

It will be recalled that the first Clinical Congress was held in this city in 1910, and that out of that meeting, largely attended by enthusiastic surgeons from all parts of the United States and Canada, came the organization of the College which this year celebrates its twentieth anniversary.

The Congress will open at 10 o'clock on Monday, October 9, with the annual hospital conference to be held in the ballroom of the Stevens Hotel. An interesting program of papers, round table conferences and practical demonstrations dealing with problems related to hospital efficiency is being prepared for presentation at this conference which will continue on Tuesday and Wednesday. The program is being prepared with a special view to interesting surgeons, hospital trustees, executives, and personnel generally.

Among the outstanding features of this year's session of the Clinical Congress will be: (1) a symposium on cancer under the auspices of the College Committee on the Treatment of Malignant Diseases on Thursday afternoon following the annual meeting; (2) a conference on fractures arranged by the College Committee on the Treatment of Fractures, on Wednesday afternoon.

A preliminary program of clinics and demonstrations is being prepared under the supervision of the Committee on Arrangements for publication in an early issue of this journal. Operative clinics and demonstrations in the hospitals will be scheduled for Monday afternoon, October 9, beginning at 2 o'clock and for the mornings and afternoons of each of the four following days. All departments of surgery will be represented in this clinical program—general surgery, obstetrics, gynecology, urology, orthopedics, and surgery of the eye, ear, nose and throat. Hospitals participating in the program are:

Alexian Brothers
American
Augustana
Albert Merritt Billings
Chicago Eye, Ear, Nose and Throat
Chicago Lying-In
Chicago Memorial
Children's Memorial
Columbus
Cook County
Evangelical Deaconess
Evangelical
Evanston
Garfield Park
Grant
Henrotin
Holy Cross
Illinois Central
Illinois Eye and Ear
Illinois Masonic
Jackson Park
Lake View
Little Company of Mary
Lutheran Deaconess
Mercy
Mount Sinai
Municipal Tuberculosis
John B. Murphy
Oak Park
Passavant Memorial
Post-Graduate
Presbyterian
Ravenswood
Michael Reese
Research and Educational
St. Anne's
St. Anthony de Padua
St. Bernard's
St. Francis
St. Joseph's
St. Luke's
St. Mary of Nazareth
Shriner's
South Chicago Community
South Shore
Swedish Covenant
U. S. Marine
U. S. Veterans
University
Washington Boulevard
Wesley Memorial
West Suburban
Frances Willard
Women's and Children's

An Executive Committee appointed by the Board of Regents to supervise the development of the clinical program, is as follows: Philip H. Kreuscher, chairman; Oscar E. Nadeau, secre-

tary; Joseph Beck, William R. Cubbins, Frederick H. Falls, Harry S. Gradle, Carl A. Hedblom, Charles E. Kahlke, Herman L. Kretschmer, Karl A. Meyer, Dallas B. Phemister, Edwin W. Ryerson, and Henry Schmitz. To this group will be added representatives for each of the hospitals co-operating in the clinical program to comprise the local Committee on Arrangements.

Two sub-committees have been appointed to supervise the program for the sections on surgery of the eye, ear, nose and throat as follows: Ophthalmology—Harry S. Gradle, chairman; Thomas D. Allen, E. K. Findlay, Sanford Gifford. Otolaryngology—Joseph Beck, chairman; Austin A. Hayden, Edward P. Norcross, S. J. Pearlman. The recommendations of this committee insure a worth while program of clinics and scientific sessions for all those who are interested in these specialties.

Special features of the clinical program will be: (1) Demonstrations at several hospitals of modern methods in the treatment of fractures, which form so large a part of the surgical work in large cities and industrial centers; (2) a series of cancer clinics demonstrating the treatment of cancer by surgery, radium and X-ray; (3) clinics in traumatic surgery demonstrating methods of rehabilitation by surgery and physiotherapy of patients injured in industrial, automobile and other accidents.

EVENING MEETINGS

The Central Executive Committee of the Congress is preparing programs for the series of five evening meetings to be held in the grand ballroom of the Stevens Hotel.

At the presidential meeting on Monday evening, following the address of welcome by the chairman of the Committee on Arrangements, Dr. Philip H. Kreuscher, the Director-General, Dr. Franklin H. Martin, will introduce the visiting surgeons from foreign countries, a large number of whom have been specially invited to attend the Congress this year. Following the address of the retiring president, Dr. J. Bentley Squier, of New York, the president-elect, Dr. William D. Haggard, of Nashville, Tennessee, is to be inaugurated. The John B. Murphy oration in surgery will be delivered at this meeting by Dr. Loyal Davis, of Chicago.

At the annual convocation of the College to be held on Friday evening, when the 1933 class will be received into Fellowship in the College, the presidential address will be delivered by Dr. William D. Haggard, and the Fellowship address by Robert Maynard Hutchins, A.M., LL.D., president of the University of Chicago.

For the sessions on Tuesday, Wednesday, and Thursday evenings, distinguished surgeons of the United States and Canada with visiting surgeons from abroad have been invited to present papers dealing with surgical subjects of timely interest. Among the speakers who will present papers are the following: George W. Crile, M.D., Cleveland, on "Clinical Problems and End-Results in the Surgical Treatment of Goiter"; Edward D. Churchill, M.D., Boston, "Tumors of the Parathyroid Glands"; Edward C. Naffziger, M.D., San Francisco, "Treatment of Exophthalmos"; George E. Brown, M.D., Rochester, Minnesota, "Thrombo-Angiitis Obliterans"; David Edwin Robertson, M.D., Toronto, "Sympathectomy in Children."

Arrangements are being made for additional sessions on Tuesday and Thursday evenings at which programs of special interest to ophthalmologists and otolaryngologists will be presented.

HEADQUARTERS—HOTELS

General headquarters for the Clinical Congress will be established at the Stevens Hotel, located on Michigan Avenue between Seventh and Eighth Streets. This hotel affords unusual facilities for all activities of the Congress, as will be remembered by those who attended the Congress in Chicago in 1929. The grand ballroom on the second floor with other large rooms on the third floor and the exhibition hall have been reserved for the exclusive use of the Congress. All of the evening sessions, the hospital conference on Monday, the annual meeting, the cancer and fracture symposia will be held in the grand ballroom. The registration and information bureau, together with the bulletin boards on which will be displayed the daily clinical program will be established in the exhibition hall in the basement, together with the Technical Exhibition.

Chicago has many fine, large hotels, several within walking distance of the headquarters hotel. A list of the hotels recommended by the Committee on Arrangements will be published at an early date. While Chicago's hotel facilities are very great and there should be no difficulty in securing first class hotel accommodations, it is advisable for those who expect to attend the Clinical Congress to reserve their hotel accommodations as far in advance as possible, as the Century of Progress Exposition will undoubtedly bring to Chicago a very large number of visitors.

The Technical Exhibition of the Clinical Congress will be located in the Exhibition Hall together with the registration and information bur-

eau. In the same room will be found the bulletin boards on which the daily clinical programs will be posted each afternoon. The leading manufacturers of surgical instruments, X-ray apparatus, operating room lights, hospital apparatus and supplies of all kinds, ligatures, dressings, pharmaceuticals, and publishers of medical books will be represented in this exhibition.

We are assured that the railways of the United States and Canada will grant especially low rates on account of the Clinical Congress in connection with the Century of Progress Exposition in Chicago. Applications for reduced fares for this meeting are pending before the various railway traffic associations.

ADVANCE REGISTRATION

The hospitals of Chicago afford accommodations for a large number of visiting surgeons, but to insure against overcrowding, the attendance will be limited to a number that can be comfortably accommodated at the clinics—the limit of attendance being based upon the results of a survey of the amphitheaters, operating rooms, and laboratories of the hospitals and medical schools to determine their capacity for visitors. It is expected, therefore, that those surgeons who wish to attend the Clinical Congress in Chicago will register in advance.

Attendance at all clinics and demonstrations will be controlled by means of special clinic tickets, which plan provides an efficient means for the distribution of the visiting surgeons among the several clinics and insures against overcrowding, as the number of tickets issued for any clinic will be limited to the capacity of the room in which that clinic will be given.

A registration fee of $5.00 is required of each surgeon attending the annual Clinical Congress, such fees providing the funds with which to meet the expenses of the meeting. To each surgeon registering in advance a formal receipt for the registration fee is issued, which receipt is to be exchanged for a general admission card upon his registration at headquarters. This card, which is non-transferable, must be presented in order to secure clinic tickets and admission to the evening meetings.